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THE EFFECT OF ILLNESS UPON EMOTIONAL DEVELOPMENT

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IT IS generally recognized that psychologic maladjustments of the adult have their origin in childhood. Specifically, it may be said that to a large extent they have their origin in the fears and resentments of childhood. It is important, therefore, to study the emotional development of children in order to determine the conditions which stimulate fears. When studying emotional reactions of children in medical clinics, one is impressed with the frequency with which fears are related to medicine. By "medical fears" we mean those stimulated by illness or therapeutic procedures, including hospitalization. Although much of the material to be presented is common knowledge, justification for devoting a paper to the subject is found in its extreme importance, in the fact that only two references can be found[1, 2] in contemporary medical literature, and in the frequency with which it is ignored in daily practice.

In order to appreciate the importance of medical fears, one must recall the nature of fear, the relation of fear to general emotional development, and the permanent damage which fears produce. Fear is one of the most important emotions. Instinctive in origin and concerned largely with self-preservation, it is stimulated whenever the feeling of security of the individual is interfered with. Love and a feeling of security, the two essentials for normal emotional development, are given the newborn by the mother. At birth the baby is completely dependent upon mother and finds complete security in her. Later he finds some security in the father, the family, and others about him. As he grows older, he slowly learns how to take care of himself and, as he develops self-reliance and responsibility for himself, de-

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pends on the parents less for security. During this period of growth, however, continuous security must be furnished; otherwise he becomes fearful.

Fear is always accompanied by resentment. When security is undermined and the normal affective relationship is disturbed, the child becomes frightened and resentful. These fears and resentments are most serious when the parents are involved, but severe fears can also be traced to physicians and hospitals because in them also rests security. The resentments, especially toward parents, lead to a sense of guilt, self-criticism, and the like. Furthermore, one must remember that all behavior is in terms of habit. If frightened enough times, the child gradually forms the habit of reacting to all situations, especially new ones, with marked fear. He is then spoken of as a fearful type of individual. Furthermore, one must remember that fears, especially the most distressing ones, may be cut off from consciousness entirely, giving rise to complexes, those ghosts of childhood which torment us throughout maturity. Fear, then, is stimulated principally as a response to the threatened security of the child, who acts instinctively in self-preservation. Secondarily, it is stimulated by uncertainty and lack of confidence.

In what way do illness, medicine, and therapeutic measures bring about these conditions? There are two reasons for the association of medicine with fear. The first is that illness has to do with the possibility of death. The second reason for the many fears stimulated by illness lies in its background of mystery and magic and its concomitant connotation of sin and punishment. Until less than a century ago diseases or death were linked with supernatural powers; illness was generally considered evidence of punishment for sin. Whenever an individual became ill or died, the illness or the death was interpreted as punishment. As is well known, this idea offered the greatest resistance to medical advancement; for example, it provided the most violent objection to vaccination. This conviction persists in the minds of a large part of the laity and is found in the minds of children. When children are asked, "Why do you get sick?" a very large percentage of clinic children and a majority of those in private practice reply, "Because you were bad." This idea is used by parents as a popular form of discipline. Whenever a child contracts a cold, for instance, a barrage of reprobation is provoked. "I told you so. You didn't wear your rubbers yesterday. You didn't mind your mother. You deserve to get sick." Such talk, coupled with the fact that all children are convinced that they are bad, even to the point of being convinced that all of the things normal children do are bad, explains the source from which comes fear in the minds of children.

This general attitude toward illness on the part of children was especially illustrated in a recent survey of the cardiac and diabetic children at the Children's Memorial Hospital. Here we had a group of children with illnesses which are likely to continue all their lives. When this group was asked, "Why do children get sick?" about 90 per cent answered, "Because they are bad." When the cardiac children were asked, "Why do you get heart disease?" they answered, "Because I ran too much." All children are told they should not run so much. The reason for this is found in study of the attitudes of the parents. In some children the replies were more complicated. This is illustrated in the case of a twelve-and-a-half-year-old girl who was referred to the psychiatric clinic because of marked nervousness during the preceding six months. When asked why she had heart disease, she replied, "It is from chorea."

"Why do you get chorea?"

"It is from nosebleeds."

This girl had had heart disease for over three years. She commonly had nosebleeds. When this occurred, she was placed in bed, and the parents, as well as herself, became apprehensive lest she develop chorea and more heart disease and die. Blood from the nose was described as "bad blood." Here we see again the relationship between illness and badness. She had been particularly nervous during the preceding six months. This dated from the time when the mother, very wisely and in a very nice way, explained menstruation and physiologic changes to her. Menstruation, however, was bleeding every month. This information, therefore, stimulated the fear that each month she might develop chorea and her heart might get worse. Menstruation had to do with "bad blood." Similar replies were obtained from the children with diabetes. When they were asked, "Why did you get diabetes?" eighteen of twenty-one children replied, "Because I ate too much sugar." Again, all children are given the impression that it is bad to eat too much sugar.

The intimate relation between illness and the fear of death with goodness and badness is illustrated by the following two cases:

W. H., a very bright boy, was causing trouble in the diabetic clinic. He refused to follow the diet, had temper tantrums, and was more or less unmanageable. He became worse following the death of his brother. He was convinced that he had diabetes because he was bad and ate too much sugar. He thought people died because they were "not as they should be." He thought he was bad and his brother was bad because of mutual sex activities which had been discovered. He felt that his brother had died as punishment for doing these terribly bad things. Other factors always enter the picture. This boy was very jealous of his brother and often wished him dead. This gave rise to

a marked sense of guilt; he thought he ought to be punished and might die for the same reason. He became frightened and resentful and refused to follow the diet. This led to punishment from the parents, and he wondered whether they liked him. This doubt, in turn, undermined his feeling of security in his parents and only added to his fears, resentments, sense of guilt, and feeling of inferiority, desire to be punished, and aggression (temper tantrums).

Another ten-and-a-half-year-old boy with diabetes was asked, "Why do children get sick?"

He replied, "God makes them sick because they do something wrong. He does it to punish them."

"Why did you get sick?"

"Because I always hated my brother; I fight him."

"What else do you do that is bad?" He confessed to stealing, sex interests, talking back, and not doing what he was told to do. When asked, "What happens to bad kids?" he replied, "They get sick and sometimes die. Then the devil gets them."

We have, then, children with illnesses which may cause their deaths and of which they are perhaps normally afraid, convinced that this illness is due to the fact that they are bad and worthless. Furthermore, these convictions have, to a large degree, been learned from their parents, in whom the child has the only real source of security in the world.

Among other emotional reactions stimulated by illness, one of the most common is infantilism. When children get sick, their parents become worried. This attitude is improved or made worse by the attitude of the physician. Being worried, parents are willing to give the child every attention. This is carried to such an extreme that children enjoy illness, and mothers are needlessly exhausted by it. The illness furnishes for the child an escape from responsibilities and creates an excuse for a reversion to his infancy. For this reason, he begins to suck his thumb, insists upon being fed, cries a great deal, often uses baby talk, and demands constant attention. All this, superimposed upon the normal fears incidental to illness, results often in an immaturity following the illness, which may take several months to erase.

Individuals do not become neurotic after they grow up. By "neuroticism" we mean the use of illness as an escape from unpleasant reality and emotional conflicts and the fear of illness without provocation. That one sees the same signs in children is illustrated by the following case.

H. B., a ten-year-old boy, was brought for examination because of headaches. Careful physical examination, including eye, ear, nose, and throat, and a check of the nervous system were all negative. Care-

ful questioning brought out that the pain was vague and sometimes localized in the middle of the forehead. It occurred in the morning, sometimes after frightening dreams, following examinations in school of which he was very apprehensive, and following disputes with other children, with whom he was very unpopular. He was very dependent upon his mother and was closely attached to her. She described similar headaches which she had had and which had been ascribed to gastrointestinal disturbances. She was sure the boy was ill because of underweight. The patient probably had some discomfort on an emotional basis. He used it as an escape from his troubles and as a means of holding the constant attention of the mother.

A great deal can be done to eliminate the harmful effects of illness pictured above by cultivating a proper attitude in the parents. When a child has a cold with a fever, he can be told to stay in bed until he has recovered, and the essential therapy carried out without frightening him, giving him constant attention, or allowing him to revert to his infancy. He can be taught the harmless nature of somatic complaints, and he can be made to see that he is using illness as a substitute for facing his problems.

One sees a great many children who have developed nervous reactions after a hospitalization. Study of these children often brings out several fears which explain their reactions. When children are placed in a hospital, especially in the charity ward, they are separated from those upon whom they have been wholly dependent and in whom they have their greatest security. This alone may be sufficient to cause emotional disturbances. It is common knowledge to pediatricians that even babies do poorly in a hospital, even though they get the most expert care, and that these same babies will thrive at home with the mother, even though the care is comparatively poor. The most probable explanation is that the affectionate and emotional relation between the baby and the mother is essential to development. Surely, from the emotional standpoint, the separation of children from their parents (and the younger the child the more important this becomes) is a serious matter. Younger children entering the hospital are commonly frightened by wrong impressions. It is not uncommon to find a child who believes he will never see his parents again. Ignorant parents often tell their children, "If you don't behave yourself, I will take you to the hospital and leave you there." Bewildered by prevarication and uncertainty, the child is then placed in the hospital, and the parents are not permitted to see him during this period. No wonder that he becomes terrified.

These reactions are well illustrated in the case of a ten-year-old girl who was brought for examination because of "spells" and extreme nervous reactions so severe that epilepsy and chorea were con-

sidered as possible diagnoses. According to the history, there was a complete change in the personality of this girl following hospitalization at five and a half years of age. At that time she was in a contagious disease ward for many weeks and was not seen by her mother except two or three times, and then through a closed glass door. This very bright little girl was able to reconstruct some of the impressions she had at that time. She thought she would never see her mother again (her father was dead). When taken to the hospital she was assured that, when the doctor had examined her, she could go right home again. After she was in the hospital a short time, some doctors and nurses came in, told her they were not going to hurt her, and proceeded to give her diphtheria toxin. A little later other doctors came in, told her they were not going to hurt her and pierced an eardrum. Later she had a mastoid operation. Here was a child, then, thinking she would never go home, finding that she could not believe the doctors and nurses who were taking care of her—all affection and security removed. The only possible reaction would be extreme fears and resentment. These were sufficiently severe to cause a change in personality so marked that encephalitis was also considered as a possible diagnosis. During the three-year period between her leaving the hospital and coming for examination, the mother reported that she would not play out with other children, that she cried a great deal, and that she was considered a nuisance in the home. The impression should not be given that the fears received by this one experience were the whole cause of her maladjustment. It was one of many problems taking its origin in the attitude of the parents and fostered by poor hospital technic. The unfortunate hospitalization was certainly a decided contributing factor.

Reactions as described in this girl were extreme. More common, however, are the milder difficulties following hospitalization. S. H., a ten-year-old boy, stammered for nine months following circumcision. He thought at that time that a radical amputation had been done. C. L., a six-and-a-half-year-old girl, had been especially nervous since her adenoids and tonsils had been removed at a "famous eastern hospital." The evening following the operation she was crying. The night superintendent of nurses told her, according to the history given to the mother, that if she did not stop crying she would be taken to the operating room and her throat would be tied up. Although three years have elapsed, the parents have been unable to induce this girl to enter a hospital, even for a visit. G. E., an eight-year-old girl, cried every time she came to the clinic. When she came to have her tonsils removed, the interne facetiously told the nurse to "give him the scissors and he would cut them out." The little girl cried bitterly and has never recovered from the experience. Milder fear reactions in

children are seen in the hospitals daily. A short time ago I was in one corner of a four-bed ward with cubicles. In the opposite corner was a two-and-a-half-year-old boy. It was very quiet for a half or three-quarters of a minute, and the child apparently thought there was nobody in the room. He began to whisper "mama" in a way which indicated terror. As soon as he found there was an adult in the room, he immediately stopped. Upon going over to this boy, I found he was lying quietly in bed with the sheets in perfect order. His pupils were very large; his pulse was rapid; his hands were clammy and wet; he was obviously terrified. The idea is sometimes expressed that children are less frightened when their parents are not allowed to visit them. It is true that they cry less and express fewer fears. It seems likely, however, that the reason that they do not cry when parents are not present is that they are too frightened to cry. It is psychologically impossible to put a child into a hospital away from his parents without alarming him, simply because he is separated from the source of his affection and security.

It may be worth while to reconstruct the psychologic reaction of a child to a simple operation, a tonsillectomy, for example. The patient is usually brought to the hospital with false assurances and persistent prevarication. He may have been told that he is going to have a party or some other ridiculous falsehood. As he enters the hospital, he notices an odor which is not especially pleasant. After going through the usual routine of admission, he is placed in bed, and the parents go home. He is surrounded by that impersonal, unemotional, disinterested attitude which has been called professionalism. Everything seems strange; he realizes that the things which have been told him by his parents are not true. He is uncertain about what is going to happen, for the prevarication of his parents has undermined his confidence in them. He automatically feels frightened. He is finally taken to the operating room, where he is greeted by an especially peculiar, unpleasant odor. Every one is dressed like a ghost. He sees the knives and instruments which the children next door have told him were used to cut off arms and legs, and in this frame of mind he can readily believe anything. He is placed on the operating table, often held down by two or three adults, and strangulated or asphyxiated into unconsciousness. Anesthetics, as given by some people, are as uncomfortable as that. There is some feeling of asphyxia, even when given by experts. Later our patient comes from the anesthesia feeling sick and possibly bleeding and vomiting. Then he is often criticized for soiling the sheet. No child ever goes through a procedure of this kind without becoming very frightened. When the importance of these fears is recognized, it will become worthy of consideration in the decision for or against an operation.

Some illnesses are unavoidable; some hospitalization and therapeutic measures are necessary. The amount of fear which children receive from these experiences, however, can be reduced greatly by the use of a proper psychologic technic. It is never justifiable or necessary to lie to a child. Children are far more reasonable and face new situation better than adults. It is better to tell a child if he is going to be hurt. The importance of this basic principle is illustrated by the boy who turned to the doctor who had opened his eardrums and said, "I hate you. You are a liar." This boy had been assured by the doctor that the latter would not hurt him before opening the eardrum. The doctor had to see him five or six times after the original visit. At these visits the patient was not hurt, the ear canal being merely wiped out. However, when the doctor assured the boy that he would not be hurt, the patient was apprehensive anyway since he knew the doctor was a liar. Therefore, he was unnecessarily frightened at these visits. On the other hand, if this boy had been told, "I have to open your eardrum. It will hurt for just a second," and then, following the opening of the ear, he had been assured that he would not be hurt any more, the patient would have had security and confidence in the doctor and would have been spared unnecessary fear. When a child goes to a hospital for tonsillectomy, as for any other operations, he will be far less afraid if he is told exactly what is going to happen. As he goes through with the procedure, although phases of it may be unpleasant, still things are going just exactly as he expected, and he has the assurance of his parents and the doctor that he is going to be well in a certain length of time and that there is no danger from the operation. His confidence and feeling of security have been maintained; consequently he has nothing to fear.

The ease with which even this psychologic procedure can go wrong is illustrated in the following case of a seven-year-old girl who had a tonsillectomy. She was told exactly what would happen. She was told that her father would go with her to the operating room and, after seating her on the table, would go out and be waiting for her in her room when she waked up. He left her on the operating table laughing and comfortable. A short time after he left the room he heard her screaming, and finally the nurse asked him to go in and help hold her while she received the anesthetic. Following the operation this girl, who had always been very cooperative, an easy patient to manage, fought every examination, had nightmares in which she screamed and fought, and was irritable at home. After some study, the cause of her severe fright was determined. When the surgeon who was to remove the tonsils went into the operating room, for reasons known only to himself—and he did not know—he decided to examine her throat again. When he took a tongue depressor and

asked her to open her mouth, the patient thought he was going to cut her tonsils out before she went to sleep. Then, not unnaturally, she began to scream and became terribly frightened.

Much can be done to lessen the fears of children in hospitals. This is done by building up their feeling of security and their confidence in their parents and the hospital staff. Whether the parents of children, especially the little ones, should be allowed to visit them but once a week is a serious question. Whether parents should not be allowed to hold their children and play with them when they come for visits is also a serious question. While it is true that it is easier to take care of children without the parents and that the patients cry less without their parents, yet, from a psychologic point of view, it is probably better for the parents to visit frequently. At the Children's Memorial Hospital a course of preparation is carried out, which greatly relieves the fear among patients. The first step is the psychologic preparation of the child for an operation. In the charity ward this is done by the head nurse who is specially trained. In the case of the private patient it should be done by the physician. This consists, as described above, in explaining to the patient what will be done. The patient often goes to the operating room the day before in order to find out what it is like. Other children who have been operated upon and who are playing nearby and are having a good time are pointed out to the patient, and he is assured that he will be doing the same thing in a few days. If he has confidence in those who tell him these things, he is far less likely to be frightened. The second step is the valuable part of the "play lady." She is an employee of the hospital staff, whose job it is to provide toys and games for the children and to spend her time in various occupational and recreational activities. All children learn before very long that when adults, especially their own parents, will sit down and play with them, they do not need to be afraid. In the same way, much of their fear in the hospital is relieved by this play. The properly trained nurse can be of great value. She can accomplish a great deal toward taking the mother's place. If the same nurse is in charge throughout a child's stay in the hospital, and if she will take the time to talk to him, play with him, and gain his confidence, the experience of hospitalization will be a far more pleasant one for him.

Often much can be done by means of pain-destroying drugs, which reduce the pain and the resultant fear. A procedure in use at the Shriners' Hospital for Crippled Children* is worthy of commendation. The night before the operation, after proper psychologic preparation, a seven-year-old child, for example, is given one grain of nembutal.

*On the service of Dr. Beveridge Moore and Dr. Harold Sofield, Shriners' Hospital for Crippled Children, Chicago, Ill.

This produces a good night's sleep. In the morning, a half hour before the operation, the dose is repeated. He goes to the operating room asleep and sleeps for six or seven hours after the operation. Vomiting is possibly reduced, or at least there is no increase in the vomiting following the operation. The relief afforded by this method from the anxiety which inevitably accompanies surgical procedure makes it worthy of mention.

During the past twenty-five years probably more well children have been frightened of illness than sick ones. This period has been characterized by a great deal of apprehension about the health of children. Every organization, from the national government to the most obscure club, is interested in children's welfare. Parents are deluged with warnings of things that may happen to their children. Even an expert in mental hygiene wrote a few years ago that all but 3 per cent of children are physically defective by the time they are six years of age.* Information conflicting in character and often superficial in nature, directions impossible to carry out or of no special value, and needless warnings of slight or imaginary deviations from the normal are given parents by the fifteen varieties of specialists in the various fields of child care. The result is that parents are in a state of confusion and apprehension. This attitude is felt by the child. From a psychologic point of view, one of the most dangerous things to teach a child is that there is something the matter with him. Yet this is done daily. Children are taught that they are too thin or too fat, or that they will grow up to be sick unless they do any one of fifty impossible things. This teaching definitely affects emotional development.

When a child feels that there is something wrong with him, he is normally frightened, and his feeling of security and self-confidence is injured. He has the tendency, if not the inclination, to fall back upon his parents for complete security and care. He becomes infantile in his emotional attitudes and develops a feeling of inferiority. He is set apart from others and feels alone and different. Feeling inferior and inadequate, he becomes resentful, antagonistic, and blames the world and those around him for his not having an equal chance with others. Often this resentment is turned upon his parents and those upon whom he is dependent but from whom he would like to gain his independence. The reaction is especially seen at adolescence. He eventually grows up a shut-in, peculiar type of individual, or an aggressive, egocentric one. All of this is commonly taught to children who are not ill. They are frightened of illness when there is nothing wrong. They are taught to be neurotic.

*_Child Care and Training_, Foegne and Anderson, p. 245.

SUMMARY

It is generally recognized that many psychologic maladjustments have their origin in the fears of childhood. Many of those fears are related to illness and medical procedures.

Fear of illness is greatly increased by its association in the minds of most children and adults with badness and punishment. It is further unnecessarily increased by prevarication on the part of parents and physicians and by failure to keep a proper relationship between the child, parent, and physician. It may be decreased to a great extent by a proper preparation of the child for medical procedures.

At the present time more well children are convinced that they have something wrong with them than sick ones. When a child is convinced there is something the matter with him physically, whether it is true or not, it leads to the cultivation of infantilism and fears, which results in feelings of inferiority and isolation of the patient. These, in turn, lead to lack of emotional development, sometimes paranoid ideas, and psychologic maladjustments in adults.

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COMMON ALLERGIC DISORDERS IN CHILDHOOD

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ACCORDING to accepted nomenclature, the allergic state is recognized and diagnosed solely on an etiologic basis. Disorders are classified as allergic only if they fulfill the etiologic prerequisite—that the manifestations of disease are ascribable to a hypersensitiveness of the tissue cells to foreign protein.

Cooke,[20] Coca,[12] Rackemann[36] and others have evolved certain clinical criteria for delimiting allergic conditions. According to Rackemann, "there are five clinical characteristics of allergic individuals:

"1. A presenting symptom which can be explained by smooth muscle spasm or by increased capillary permeability.
2. The occurrence of one or several other allergic manifestations.
3. A positive family history of allergy.
4. The presence of positive skin tests.
5. The presence of blood eosinophilia."

In addition he accepts as proof of the allergic nature of the disease:[35]

"1. The disease manifests itself when an individual comes in contact with a particular substance.
2. The symptoms disappear when this contact is broken.
3. The symptoms can be explained on a pathological basis as noted under number one of the above series of five characteristics."

In spite of such tabulated aids it is not always possible to allocate with certainty a number of clinical conditions either to the allergic or to the nonallergic category. The manifestations which are generally recognized as allergic in nature are asthma, hay fever, vasomotor rhinitis, infantile eczema, neurodermatitis, urticaria, and angioneurotic edema. Other conditions which have been included in the allergic group by a number of workers are Henoch's purpura, canker sores, gastrointestinal upsets, idiopathic colitis, migraine, enuresis, idiopathic convulsions, and certain types of arthritis accompanied by other allergic manifestations.

This paper will be confined to a consideration of the group of disorders which is generally recognized to be definitely allergic in nature.[3] Our methods of study and treatment of each condition will be illustrated from case reports drawn from the pediatric allergy clinic at New York Hospital.

The history and physical examination of a young patient requires two clinic visits. A general pediatric history, physical examination,

From the Pediatric Allergy Clinic, New York Hospital.

laboratory and roentgenographic examination are initiated during the first visit. On the second visit an allergic history is obtained, and special examinations are performed if indicated.

FAMILY HISTORY

It is the consensus of opinion that children inherit a susceptibility to sensitization and that individuals and families who will have allergic disorders are predetermined according to Mendel's law.[1]

It is generally agreed that inheritance of an allergic manifestation is not specific. Offspring of asthmatic parents will not necessarily have asthma but may acquire vasomotor rhinitis, atopic dermatitis, hay fever, or perhaps one of those "masked allergic manifestations" mentioned by Spain.[53]

In this series the age of onset in 122 patients having a unilateral family history of allergy was 3.87 years. The age of onset in 114 patients with a negative family history was 3.7 years and in 36 patients having a bilateral family history, 2.9 years.

The family history should include a note concerning the occupation of each member of the household. We recall one child who developed hypersensitiveness to sawdust, whose father was a woodworker in a mill, and another child with asthma due to horse epithelium whose father was a groom. The mother of another asthmatic child, five years old, who was hypersensitive to certain cosmetics, conducted a beauty parlor in her home.

Sensitization of the offspring through the placental circulation is probably the mode of transmission of anaphylaxis in animals. Ascoli[4] and others have demonstrated that, while it is not the usual mode of transmission of hypersensitiveness in man, it is possible for a child to become sensitive by means of the placental circulation.[42] When an allergic infant is the patient, an inquiry should be made into the habits of the mother during gestation. It is surprising to note the frequency of dietetic idiosyncrasies during pregnancy; there may occasionally be a connection between these overindulgences of the mother and the allergic manifestations in the child.

DIETARY HISTORY

Coke,[16] Donnally,[22] Ratner,[41] and others have suggested the possibility that through the medium of breast milk children become sensitive to foods eaten by the mother. This statement is based on the fact that proteins ingested by the mother appear unchanged in the breast milk. Since we know that the gastrointestinal tract is permeable to unaltered proteins,[6, 51, 56, 57] it would appear that the likelihood of sensitization of children by means of breast milk is at least a remote possibility. Furthermore, an infant already hypersensitive to some food may receive small amounts of the specific antigen by way of breast

milk. It is important for this reason to obtain a detailed feeding history of the mother and of the patient during his first year of life.

In older children there is a temptation to regard delicacies and exotic foods as possible offenders. In our experience, unusual foods or those rarely taken are seldom the cause of allergic manifestations. Food allergy is more likely to be due to some common food constantly in the diet.

ENVIRONMENTAL HISTORY

Numerous investigators have succeeded in sensitizing animals by having them inhale specific dusts.[42, 44] Sulzberger and Vaughan[54] obtained positive reactions in passively sensitized sites on nonallergic subjects by blowing the specific protein into the nose. One should, therefore, take a careful inventory of all possible sources of inhalants in the child's bedroom, including fur and cloth toys.

The relation of psychobiology to allergy as an important secondary cause of allergic manifestations is most interesting and has not been thoroughly investigated. For example, one child succumbed to an asthmatic attack when punished. The asthmatic attacks in this child could not be distinguished in appearance or on examination from a paroxysm due to exposure to the specific protein in a hypersensitive individual. It is not unusual to note a child with periodic attacks of paroxysmal dyspnea who has lived with or near a relative or playmate with asthma and in whom it is impossible to demonstrate hypersensitiveness. One must suspect but cannot prove that these children have asthmatic manifestations of intrinsic or reflex origin. Children sometimes resort to asthmatic attacks to express latent hostility or to evade reality.

SKIN TESTS

The routine series of skin tests comprises sixty allergens which require for their performance four clinic visits. Repetitions and additional tests not in the regular series require an average of two more visits. Appraisal of the clinical significance of positive reactions is made by clinical test with specific material during a number of succeeding visits.

Intracutaneous testing in our opinion is the method of choice. The same concentration of allergens measured in milligrams of total nitrogen per cubic centimeter is used in this children's clinic as in adult clinics. If there is any difference in response to cutaneous tests between children and adults, it is that the former give fewer constitutional reactions than the latter. The local blocking mechanism may function more completely in children than in adults, thereby preventing or reducing to a minimum the spilling over of antigen into the circulation.[31] In adults the introduction of a protein to which the

individual proves sensitive, either cutaneously or intracutaneously, results in a wheal which becomes progressively larger during a period of about twenty minutes. In children, however, the wheal starts as in adults but usually, in a shorter period of time, attains a relatively small maximum size. This fact together with the method of testing may explain the absence of constitutional reactions observed in our clinic.

In the performance of an intracutaneous test, the smallest amount of antigen which will produce a visible wheal is injected. This quantity is less than 0.01 c.c. A positive reaction by this method must be irregular in outline and should be surrounded by an area of erythema. The actual size of the wheal is of less importance.

In view of the difference in reactivity of the skin in different individuals,[2, 58] we have found it feasible to group our patients into three classes based on the response of the skin to tests.

1. "Normal"—skin which will give definite positive and definite negative reactions.
2. Hyposensitive—skin which reacts slightly to the most potent allergen to which the patient proves sensitive.
3. Hypersensitive—skin which gives good reactions to almost all tests but seldom gives an outright negative reaction.

The "normal" skin, Group 1, usually reacts well to either scratch or intracutaneous tests. Hyposensitive skins, Group 2, are almost impossible to test by the scratch method. Group 3 skins offer an excellent opportunity for the use of the scratch method, and in the latter cases it is frequently necessary to resort to passive transfer tests.

Since an appreciable number of clinically positive cases, usually with hyposensitive skins, might be missed if the scratch method were employed and since with proper technic the risk of intracutaneous testing is negligible, the latter is routinely employed in this clinic.

Inasmuch as the scratch method has many advocates, a duplicate series of scratch and intracutaneous tests on 172 consecutive patients with allergic disorders has been completed and is recorded in Table I.

The routine list of allergens is arranged in the order of frequency with which reactions were obtained by the intracutaneous method. Allergens giving no positive reactions by either method, such as gelatin, cabbage, celery, lettuce, plum, raisin, and others, are omitted because of lack of space. For the same reason various feathers, nuts, meats, and fish are grouped in the table although in each instance a number of feathers, nuts, meats, and fish were tested separately.

The first column is a list of all positive reactions obtained by the intracutaneous method. The second is a list of those reactions in

TABLE I

SCRATCH VS. INTRACUTANEOUS TESTS—172 PATIENTS

DILUTION MG. TOTAL N. PER C.C.	ALLERGEN	INTRACUTANEOUS			SCRATCH		
		ALL POSITIVE REACTIONS	SIGNIFICANT POSITIVES	PSEUDO-POSITIVES	ALL POSITIVE REACTIONS	SIGNIFICANT POSITIVES	PSEUDO-POSITIVES
0.1	Dust	85	--	--	29	--	--
0.1	Feather	73	51	22	22	14	8
0.01	Ragweed	65	21	44	65	19	46
0.03	Kapok	29	20	9	13	11	2
0.01	Grass pollen	29	5	24	28	3	25
0.03	Cat epithelium	24	6	18	24	5	19
0.1	Pyrethrum	22	2	20	11	3	8
0.01	Egg white	20	13	7	23	12	11
0.1	Bean, mixed	19	2	17	8	0	8
0.1	Strawberry	18	2	16	9	1	8
0.03	Orris root	18	5	13	13	2	11
0.1	Chocolate	18	3	15	5	1	4
0.3	Milk	16	7	9	6	3	3
0.03	Dog epithelium	16	2	14	11	2	9
0.03	Silk	14	9	5	13	8	5
0.1	Wheat	14	6	8	9	3	6
0.1	Banana	14	1	13	14	0	14
0.1	Carrot	14	0	14	0	0	0
0.01	Horse epithelium	13	6	7	13	4	9
0.1	Oat	13	5	8	6	2	4
0.03	Fish	13	7	6	9	6	3
0.1	Orange	13	0	13	16	0	16
0.1	Sheep wool	13	3	10	4	1	3
0.1	Goat (mohair)	11	2	9	2	0	2
0.1	White potato	11	1	10	11	0	11
0.1	Meats	11	3	8	6	0	6
0.1	Rye	11	1	10	6	1	5
0.1	Rice	10	2	8	1	0	1
0.1	Corn meal	8	0	8	5	0	5
0.1	Pea	7	0	7	5	0	5
0.1	Tomato	7	0	7	5	0	5
0.01	Flaxseed	6	1	5	6	1	5
0.1	Spinach	5	0	5	11	0	11
0.01	Nuts	5	2	3	8	2	6
0.1	Apple	4	1	3	5	1	4
0.01	Rabbit	4	1	3	7	1	6
0.1	Barley	2	0	2	5	0	5
0.01	Mustard	2	0	2	16	0	16
0.1	Tea	2	0	2	1	0	1
		579	190	304 85 dust	351	106	216 29 dust

Twenty-five patients listed in columns 1, 2, and 3 gave no positive reactions. Of these, nineteen had asthma of infectious origin.

Twenty-nine patients listed in columns 4, 5, and 6 gave no positive reactions. Of these, sixteen had asthma of infectious origin.

column one found by clinical test to be significant. The third is a list of reactions having no known significace. Columns four, five, and six refer in the same manner to reactions obtained by the scratch method.*

*Arlington Chemical Company intracutaneous test solutions and scratch test materials were used in all of the tests recorded in Table I. At this point we should like to express our appreciation to the Arlington Chemical Company for lending us one of their technicians to make the scratch tests recorded in this table. The conscientious and meticulously painstaking work of Miss Benedict during the past eighteen months was of inestimable value.

CLINICAL TESTS

Multiple positive reactions were obtained by both methods of testing. The majority of such reactions do not necessarily parallel clinical sensitivity. Therefore, all positive reactions were tested clinically in order to appraise their significance. For instance, in the case of suspected inhalant sensitivity, the child is isolated and asked to handle the specific article or material for a period of at least thirty minutes. Frequently there is an immediate conjunctival injection and irritation and moderate rhinorrhea. This is considered to be a positive clinical test. At other times the child may have no immediate reaction but may have an attack of asthma on the night of the test. If this is repeated several times with the same result, the inhalant is judged significant. When there is suspicion of food sensitivity the child is instructed to report at the hospital in the early morning, is fed the suspected food, and is observed during the remainder of the day. Urticarial wheals, angioneurotic edema, erythema multiforme, and acute gastrointestinal upsets are considered markedly positive reactions. Swelling of the nasal mucosa, coughing, vague gastrointestinal discomfort, repeated swallowing, and frequency of urination are thought to be milder responses. Delayed reactions are likely to consist of an exacerbation of the chief complaint and are not likely to occur when moderate amounts of the food are used for the trial.

With other patients, direct clinical trial is unsuccessful, but the removal of a hair or kapok mattress or feather pillow, stuffed chair, rug or similar articles from the child's bedroom may result in freedom from symptoms, which may recur when the material is reintroduced.

By use of such methods, one or more allergens are located and may be said with reasonable assurance to be directly implicated in the child's disorder. All allergens called significant in the above chart were diagnosed and confirmed in this manner. These clinical trials are procedures which are time consuming but well worth the effort. They frequently take months to complete.

COMPARISON OF THE INTRACUTANEOUS AND SCRATCH TESTS

It will be noted in Table I that the intracutaneous method gave 304 reactions of no known significance (column 3) as contrasted to 216 pseudoreactions by the scratch method (column 6). This relatively small number of false positive reactions by the intracutaneous method is contrary to the usual experience of allergists and is probably due to our method of making intracutaneous tests, that is, by injecting minute amounts of allergenic material within the layers and not beneath the skin. A convincing explanation of the pseudoreaction is not known.

According to the figures in Table I, had only scratch tests been done, 84 clinically positive reactions would have been missed. Our

attention is called to certain allergens such as ragweed, grass, cat hair and others which are prone to give pseudoreactions. It will also be noted that allergens such as rye and sheep wool, giving pseudoreactions by the intracutaneous method, are frequently different from those such as mustard and others, which cause false positive reactions by the scratch method.

Dust reactions have not been placed in the clinically significant columns. To do this, of course, is fallacious.[18, 46, 47, 64] The exact meaning of so many markedly positive dust reactions by either method of testing is not known. Dust may contain an unknown specific allergen, but it seems more likely that its reactions are due to some common inhalant constituent such as hair or feathers. Positive dust reactions are considered by us to be of value only so far as they stimulate a further search for the offending inhalant present in the room from which the dust was collected.

THE PRAUSNITZ-KÜSTNER REACTION[33, 50, 65]

The passive transfer test is feasible clinically and more than one hundred children are tested yearly with this method. No insurmountable or impractical details have been found. In performing these tests it has been found advisable, in view of the occasional normal person who fails to accept transfer of hypersensitivity, to test each prospective recipient with serum known to contain reagin.

During the course of testing a large number of subjects by means of the passive transfer reaction, we have noted that pseudoreactions, just as with direct testing, are common and that we occasionally obtain positive passive transfer reactions to allergens which fail to give positive reactions by direct methods.[6]

In the majority of subjects acting as recipients of passive transfer serum, in whom a positive reaction is obtained, it is possible by feeding the specific food[8, 51, 57] or by applying the specific inhalant to the nasal mucosa[54] to obtain a positive response in the sensitized area of skin. It is also a fact that contralateral injections of sufficient quantities of allergen will elicit positive responses in sensitized areas.[24]

THE PATCH TEST[55]

This popular method of testing for contact irritants has not proved to be as valuable in children as it is reported in adults. Children with dermatitis have been routinely tested with this method with the various chemicals found in lotions, ointments, and cosmetics and to oils of certain common allergens[39, 40] whenever it seemed to be indicated. The patch test is watched daily for five days. A positive response is inflammatory and is always delayed. Vesiculation is observed in markedly positive reactions. Wheals which appear immediately and fade within an hour or two are considered negative reactions to the patch test and should be interpreted as scratch or intracutaneous reactions.[28]

TABLE II

SUMMARY TABLE

		NUMBER OF PATIENTS	AVERAGE AGE AT ONSET	AVERAGE AGE AT FIRST VISIT	AVERAGE DURATION TREATMENT MO.	POSITIVE FAMILY HISTORY (%)	HISTORY INFANT ECZEMA (%)	POSITIVE SINUS (%)	MALES (%)	RESULT A	RESULT B	RESULT F
Asthma	Food	12	1.8	4.1	16.0	100	92	80	40	4	1	7
	Food and inhalant	11	2.4	6.2	13.0	55	55	81	57	3	7	1
	Inhalant	83	4.2	7.7	12.0	63	40	68	70	49	14	20
	Infection	59	3.9	7.1	16.0	50	25	61	77	34	13	12
	Infection and protein	14	3.5	7.5	17.0	71	57	71	77	4	6	4
	Unknown	13	3.3	6.1	9.5	84	23	53	66	4	1	8
	All asthma	192	3.7	7.0	14.0	62	40	67	70	51%	21%	28%
Hay fever	Seasonal hay fever	35	6.5	9.0	---	77	40	70	34	17	14	4
	Vasomotor rhinitis	10	4.2	8.6	8.5	90	40	50	90	3	2	5
Dermatitis	Infantile eczema	14	0.29	0.9	7.0	21	--	62	--	7	6	1
	Neurodermatitis	44	3.1	6.5	8.5	50	85	40	--	22	10	12
	Urticaria	11	2.9	5.5	6.0	36	27	72	--	3	4	4
	All dermatitis	69	2.5	5.5	7.9	38	75	43	--	46%	29%	25%
	All patients	275	3.7	6.9	12.0	58	42	61	--	48%	25%	27%

Seventeen patients with hay fever also have asthma.

Fourteen patients with neurodermatitis also have asthma.

Results: A. No symptoms for at least six months.
B. 50 per cent relieved.
F. All others.

REVIEW OF ALLERGIC DISORDERS

The allergic conditions reviewed in this paper are asthma, hay fever, infantile eczema, neurodermatitis, and urticaria. They are presented in Table II.

ASTHMA

From an etiologic point of view asthma in children may be divided into three distinct types, each presenting a fairly characteristic clinical picture: first, those patients sensitive to an inhalant or to food or to both: second, children with negative skin tests whose asthma is thought to be of infectious origin; and third, children in whom infection and extrinsic protein sensitization play more or less equally important rôles.

Children of the first type give a history of periodic well-defined paroxysms of dyspnea each lasting a comparatively short time. The attacks are abrupt in onset and in recovery, and the patients are usually well between paroxysms. Attacks are often environmental but never seasonal unless caused by pollen. Secondary excitants, such as upper respiratory infections, undue cold or heat, or emotional disturbance, are likely to precipitate an attack.[4] Such excitants apparently act in a nonspecific manner, lowering the threshold of resistance or otherwise disturbing the allergic equilibrium, thereby enabling a relatively small amount of specific antigen to produce a reaction.[62] These children in our experience are usually mentally and physically above average. We hope to present data in support of this statement at a later date. Infection plays no direct part in their asthma. Elimination or hyposensitization results in clinical relief in many.

Of 275 allergic patients under consideration, 192, or 70 per cent, had asthma. Of the asthma patients, 106, or 55 per cent, were of the type just described (Table III).

TABLE III

GROUP 1 ASTHMA PATIENTS

CAUSE	NUMBER OF PATIENTS	AVERAGE AGE OF ONSET	AVERAGE AGE AT FIRST VISIT	AVERAGE DURATION TREATMENT, MO.	POSITIVE FAMILY HISTORY	MALES	HISTORY INFANT ECZEMA	RESULT		
								A	B	F
Food	12	1.8	4.1	16	12	10	11	4	1	7
Food and inhalant	11	2.4	6.2	13	6	9	6	3	7	1
Inhalant	83	4.2	7.7	12	52	57	51	49	14	20
Total	106	3.8	7.1	13	66%	71%	64%	52%	20%	28%

The inhalants responsible in Group 1 patients were:

Feather	51	Orris root	4	Dog epithelium	3
Kapok	23	Grass pollen	4	Pyrethrum	1
Horse epithelium	12	Flaxseed	3	Quince seed	1
Ragweed	13	Silk	2	Rabbit epithelium	1
Cat epithelium	6	Goat epithelium	2		

Twenty-three children, or 27 per cent of the patients in whom inhalants played a known part, were clinically sensitive to kapok. We believe that this fact is worthy of emphasis because of the frequency with which allergic children are given kapok mattresses and pillows as substitutes for hair and feather articles.[7] It has been our experience that the safest nonallergic upholstery stuffing material is cellulose fiber or rayon waste.[11]

The foods responsible in Group 1 asthmatic patients were:

Egg	11	Nuts	2
Cereals	7	Meats	3
Fish	5	Potato	1
Milk	4	Fruits	1

It is interesting to note that in only twelve children, or 6 per cent of the cases, was the asthma due to food alone.

We offer the following case histories to illustrate this type of asthma. Colds with each patient acted as secondary excitants. It will be noted that when the specific antigen was removed, exposure to any or all of the secondary excitants was not followed by wheezing or asthma.

CASE 1.—Food. A male child, two years old, reported to the clinic with a history of asthma for the preceding twelve months, during which he had five attacks. Paroxysms occurred during day or night, winter or summer. Several followed colds. There was a maternal family history of allergy. He had had infantile eczema, relieved when he was weaned. Intracutaneous tests directly and by passive transfer gave markedly positive reactions to egg. The child had been on an egg-free diet for the past eighteen months and had but one attack, following the ingestion of frozen custard at a party. Since he has been on the diet, colds have not been accompanied by asthma.

CASE 2.—Inhalant. A male child, four years old, reported to the clinic with a history of asthma for the preceding three years. The onset was frequently associated with severe coryza. A maternal family history of allergy was obtained. Intracutaneous and scratch tests to sixty allergens were negative except to quince seed. A positive reaction to quince seed was also obtained by passive transfer. On questioning, it was found that the mother used mucilage of quince to set waves in her hair and frequently applied some to the child's head. This material was eliminated from the household and the child has had no asthma during the past eight months.

The second group of asthma patients presents a different picture. These children almost invariably have a cold for a day or so, frequently accompanied by fever, followed by wheezing respiration which lasts a week or longer. There are seldom any paroxysms of dyspnea

although they may occur. Attacks occur chiefly in the winter although they may accompany a summer coryza. Many give entirely negative skin tests (in this series 37, or 62 per cent).

TABLE IV

GROUP 2 ASTHMA PATIENTS

CAUSE	NUMBER OF PATIENTS	AVERAGE AGE OF ONSET	AVERAGE AGE AT FIRST VISIT	AVERAGE DURATION TREATMENT, MO.	POSITIVE FAMILY HISTORY	MALES	HISTORY INFANT ECZEMA	SINUS POSITIVE	RESULT		
									A	B	F
Infectious	59	3.9	7.1	16	50%	61%	25%	77%	34	13	12

In general, an attempt is made to remove foci of infection. We are inclined to adopt a position of watchful waiting with regard to the frequent sinusitis unless it is quite extensive.

Although we recognize the viewpoint is open to controversy, we believe that colds in these children, filtrable viruses notwithstanding, may be due to the same excitant that causes the asthma and that this excitant is bacterial in origin. The object of our treatment is to relieve the child of head colds with the hope that success will be marked by an absence of asthma. With this idea in view, our treatment consists of administering a nonspecific catarrhal vaccine (made by Eli Lilly and Company, Lederle Laboratories, Inc., Parke, Davis & Company, and others). This treatment is continued over a period of several years. It is not unusual to obtain a severe exacerbation of asthma following an injection. When this occurs after successive injections, the vaccine is diluted 1:10. In rare instances it has been necessary to dilute the material 1:100. When diluted vaccines are necessary, the maximum dose maintaining the child free from asthma is frequently very low.

We have not seen a child in this group who was relieved of colds by this treatment have an attack of asthma. However, the converse does not hold true; that is, with a number of children we arrive at a dosage of vaccine that will maintain them free from asthma but does not entirely rid them of upper respiratory infections.

We have purposely selected a child with an early onset to illustrate the infectious type of case in order to refute a common belief, namely, that very young children do not have asthma solely of infectious origin.

CASE 3.—A male child, eighteen months old, had a history of a paroxysm of dyspnea following a cold five months before admission to the clinic. There were a number of wheezing spells during the interim. Four days before reporting to the clinic he had another paroxysm following coryza, after which he wheezed two days. The family history was negative for allergy. He had no other allergic manifesta-

tions. All skin tests were negative. The only treatment was a course of stock vaccine, which is still given at monthly intervals although the child has had no asthma during the past two years. One head cold last winter was not accompanied by asthma.

The third type of asthmatic child presents a combination of those types in Groups 1 and 2. An attack may start with a real paroxysm of dyspnea lasting anywhere from a few minutes to hours, followed by wheezing respiration lasting a week or more or even until the next paroxysm. The attacks may or may not start with a cold but usually do. Sinusitis is a frequent finding. Children of this type have a sensitization to some protein plus a strong infectious factor, and each must be treated successfully before the child becomes clinically free from symptoms. Of all allergic children these are usually the sickest, and treatment is most difficult. A typical child within this group is underweight, barrel chested, and slightly stooped. His face is pale and apprehensive. The respiration is shallow, labored, and wheezing. He is chronically ill and cannot participate in many childhood activities.

TABLE V

GROUP 3 ASTHMA PATIENTS

CAUSE	NUMBER OF PATIENTS	AVERAGE AGE OF ONSET	AVERAGE AGE AT FIRST VISIT	AVERAGE DURATION TREATMENT. MO.	POSITIVE FAMILY HISTORY	MALES	HISTORY INFANT ECZEMA	POSITIVE SINUS	RESULT		
									A	B	F
Infection protein	14	3.5	7.5	17	71%	71%	43%	77%	28%	44%	28%

To illustrate this type of asthma we present the following case report:

CASE 4.—A female child, aged six years, reported to the clinic with a history of asthma for the preceding five years. Following pertussis at nine months of age, a cough persisted for three months. At the age of twelve months, the child awakened one night with a paroxysm of dyspnea. She had, when she reported to the clinic, an attack of asthma every three weeks, lasting from two to seven days.

She has had urticaria a number of times. There was a maternal family history of allergy, A roentgenogram of the sinuses displayed diminished aeration of the right ethmoids, both antrums, and the right sphenoid. Skin tests by scratch and intracutaneous methods gave positive reactions to chicken, duck, and goose feathers.

Vaccine and elimination of feathers from the bedroom and hyposensitization with feather mixture have maintained the child free from asthma for the past year although she has very shallow respiratory excursions, a markedly decreased vital capacity and dyspnea on slight exertion. The ultimate prognosis is bad. We are inclined to believe that had this child been treated allergically four or five years ago, she would have escaped the emphysema that will probably incapacitate her for the rest of her life.

Thirteen children, or about 6 per cent of our series, are marked "cause unknown" after an average attendance of about ten months.

TABLE VI

ASTHMA—CAUSE UNKNOWN

CAUSE	NUMBER OF PATIENTS	AVERAGE AGE OF ONSET	AVERAGE AGE AT FIRST VISIT	AVERAGE DURATION TREATMENT, MO.	POSITIVE FAMILY HISTORY	MALES	HISTORY INFANT ECZEMA	POSITIVE SINUS	RESULT		
									A	B	F
Unknown	13	3.3	6.1	9.5	84%	53%	90%	66%	30%	9%	61%

A number of children are seen at the clinic with a history of asthma in whom skin tests give no useful information. In investigating such patients, the occupation of each member of the household is considered with regard to the possibility of someone carrying home an unusual or even a common inhalant allergen.

Certain allergens such as orris root, silk, flaxseed, glue, and others require a widespread search. However, since the child's bedroom affords the most likely location of any considerable amount of specific inhalant antigen, we devote most of our time to this relatively small part of a home. Our first procedure is to eliminate inhalants as far as possible from the sleeping quarters. This is accomplished by removing all furniture from the room and painting the walls and floor. The child is allowed an army cot to sleep upon, with cotton blankets and sheets and no pillow. Pets and stuffed toys are banished.

Should the child become symptom-free in this environment, one comfortable accessory after another is readmitted until the offending articles are disclosed. Using this method the cause of asthma in a majority of cases not diagnosed by skin tests is revealed.

In cases in which this method is unsuccessful, elimination diets such as those constructed by Cobb,[15] Rowe[45] or Hopkins, Waters, and Kesten[26, 66] are tried. Dietetic experiments usually extend over a period of many months. We have found that with ordinary care and attention paid to the caloric value, vitamin and inorganic content, the nutrition and well-being of the child is not seriously disturbed. We should add that an attempt, frequently unsuccessful, is made to bar cosmetics of all kinds from the entire household during a period of at least two weeks, and we introduce so-called hypoallergic cosmetics whether or not we have proved ordinary cosmetics offensive.

The group of thirteen patients recorded in Table VI remained undiagnosed in spite of all efforts along these lines.

HAY FEVER

Hay fever or hyperesthetic rhinitis, both seasonal and perennial, is a common allergic manifestation among hypersensitive children. Sea-

sonal hay fever is a subject of such interest and with so many controversial angles that it is wholly beyond the scope of this paper to discuss it in any detail.

TABLE VII

SEASONAL HAY FEVER

NUMBER OF PATIENTS	AVERAGE AGE OF ONSET	AVERAGE AGE AT FIRST VISIT	POSITIVE FAMILY HISTORY	MALES	POSITIVE SINUS	DUE TO			RESULT		
						GRASS	RAGWEED	G. AND R.	A	B	F
35	6.5	9.0	77%	57%	70%	7	24	4	17	14	4

In the neighborhood of New York City, seasonal hay fever occurs during three periods. The first extends from March through May, a period in which trees pollinate. The second starts about May 1 with the pollinating of sweet vernal grass and lasts through the prolific pollination of the other grasses, terminating around the end of July. The third period, from August 15 to November or until freezing weather begins, corresponds to the pollinating time of weeds and many flowers.

Not any of the children considered in this series had their hay fever during the tree season: in 20 per cent hay fever was due to grass pollen, 68 per cent, to weed pollen, and 12 per cent, to grass plus weed. We believe that grass-sensitive patients are more successfully treated with a five grass mixture than with timothy alone[34] and that short ragweed will relieve the vast majority of patients susceptible to weed pollen. During the past two years between July 20 to August 7, we have noted massive quantities of pigweed pollen in the air. At this time we cannot make any statement about the clinical significance of this new menace to the hay fever victim. Since the period of pollination occurs at a time when the New York sufferer from grass or ragweed hay fever is free from symptoms, we anticipate no great difficulty in obtaining data to report at a later date.

In treating hay fever patients, as an average working rule, the higher the dosage of specific pollen solution attained when the pollinating season starts, the better the result will be. Except in a few hypersensitive patients we try to reach a top dose of 0.5 c.c. of a dilution containing 0.4 mg. nitrogen per cubic centimeter. It is interesting to note the brief duration of the immunity acquired even after such relatively large doses. A child receiving 0.5 c.c. of a dilution containing 0.4 mg. nitrogen per cubic centimeter without any reaction will not tolerate one-tenth of that dose six weeks later if no injections are given during the interim.

It has been a constant finding over a number of years that children successfully treated for hay fever, particularly by the perennial method, rarely have winter colds. We have no explanation for this fact.

VASOMOTOR RHINITIS OR PERENNIAL HAY FEVER

We believe that we are less successful in our treatment of this distressing condition than of any other allergic manifestation. Due to localization of all symptoms in the nose, many patients before reporting to the clinic have had repeated nasal operations. We are inclined to state dogmatically that surgical intervention and topical treatment give no lasting relief.

The nasal mucosa presents a characteristic appearance, pale, boggy, edematous, and often with polypoid degeneration. A roentgenogram of the sinuses in all of the patients revealed a markedly thickened mucosa, frequently thickened to such an extent in part of its periphery that it gave a polypoid appearance.

The treatment is elimination or hyposensitization of implicated proteins and a course of stock vaccine. In the occasional strikingly successful case food is likely to be the offender.

DERMATITIS

In this series eczema and urticaria are considered under this heading. Forty-four children in our series reported to the clinic with eczema as their chief complaint. In addition, fourteen children with asthma also had eczema.

We recognize three types of eczema, infantile eczema, neurodermatitis and dermatitis venenata, the latter a contact irritation phenomenon of controversial classification usually treated in the dermatology clinic.

TABLE VIII

DERMATITIS

DIAGNOSIS	NUMBER OF PATIENTS	AVERAGE AGE OF ONSET	AVERAGE AGE AT FIRST VISIT	AVERAGE DURATION TREATMENT, MO.	MALES	POSITIVE FAMILY HISTORY	HISTORY INFANT ECZEMA	CAUSE			RESULT		
								INHALANT	FOOD	UNKNOWN	A	B	F
Infant eczema	14	0.29	0.9	7.0	9	3	--	--	12	2	7	6	1
Neurodermatitis	44	3.1	6.5	8.5	18	21	38	17	15	12	22	10	12
Urticaria	11	2.9	5.5	6.5	3	4	3	1	7	3	3	4	4
Totals	69	2.5	5.4	7.9	43%	40%	74%	26%	50%	24%	46%	30%	24%

Infantile eczema starts with a few papules and vesicles, usually on the cheeks, which gradually coalesce until there is a raw red surface covered with crusts formed by oozing serum. The inevitable scratch-

ing results in bleeding patches and frequently secondary infection. The eruption spreads to the scalp, upper and lower extremities and often to the trunk. These children are less than a year old. The cause is almost always a food although rarely an inhalant may be responsible.

The sequence of events leading up to asthma frequently starts with infantile eczema. Many of our asthmatic children give a past history of infantile eczema, which persisted beyond the second year, gradually changing its appearance until it assumed the characteristics of neurodermatitis. Then, all too frequently, hay fever and asthma supervened. It is our clinical impression that allergic treatment of eczema in infancy may render a child less likely to run the gamut of allergic manifestations terminating in asthma as he grows older. About 40 per cent of the asthmatic children in this series gave an antecedent history of infantile eczema.

Thirteen of the fourteen patients with infantile eczema were hypersensitive to various foods. One was neither diagnosed nor helped.

Our local treatment has been confined to tar ointments, and we have found most useful a tar, starch, and zinc oxide combination in a vanishing cream base.[32] In cases in which lanolin is contraindicated a proprietary hypoallergic tar cream has been used successfully.[29]

The foods responsible in the infantile eczema patients were:

Egg	8	Meat	2	Unknown food	2
Wheat	2	Fish	2	Peas	1
Milk	2	Spinach	2	Oats	1

It is interesting to note that all of the above children were tested solely by means of passive transfer, not primarily because of their age, but because we were unable to find an area of skin clear enough to test directly on any of them.

In feeding allergic infants cemac[17] and sobee[27] have been found useful in selected patients. It has been our experience that milk-sensitive children fare better on milk-free diets than on boiled evaporated milk or the so-called hypoallergic milk products. We have found that hypoallergic milk has an advantage over whole cow's milk when milk is reintroduced into the diet of patients who have been on a milk-free diet for a long time and in patients hyposensitized to milk. Children should be kept on diets eliminating the foods to which they are sensitive for a year or more, after which they can frequently eat moderate amounts with impunity.

NEURODERMATITIS[52]

We prefer to call the familiar flexural eczema "neurodermatitis." The appearance of this lesion is characteristic: a widely disseminated, scaly, nonvesicular eruption on greatly thickened, lichenized and discolored skin. Although it commonly localizes on the flexor aspects of

the elbows and knees, it is frequently distributed over the entire body. The children give a family history of allergy in about 50 per cent of the cases. Females predominate almost two to one. Skin testing is successful by the scratch or intracutaneous methods. Patch tests are never positive in these children.[60]

Forty-four, or 65 per cent, of our patients with dermatitis were of this type. It will be noted by reference to Table II that the average age of onset was 3.1 years as contrasted with 0.29 years in infantile eczema.

Seventeen of the forty-four patients had inhalant sensitivity. The offending proteins were:

Silk	9	Orris	2
Feather	6	Kapok	1
Wool	2		

The dermatitis in fifteen was caused by food hypersensitiveness:

Egg	7	Cereal	4	Nuts	1
Fish	5	Vegetable	3		
Milk	4	Fruit	2		

Of the twelve patients whose cases were not diagnosed after trial periods of elimination diets and search for inhalants, six were relieved of all symptoms, one was greatly benefited, and five showed no improvement.

Cases of neurodermatitis afford an excellent demonstration of the patience and intelligent cooperation required on the part of the physician, the patient, and the parents. The following case report is offered as an illustration:

CASE 5.—A female child, ten years old, first reported to the clinic in August, 1933. She gave a history of having had a skin eruption since the age of six months. There was a paternal history of allergy. At the age of four the child had a paroxysm of dyspnea. The mother recalled that at the time of the first paroxysm, the appearance of the skin lesion had changed to a scaly, nonvesicular eruption covering the entire body. She has had three or four asthmatic attacks yearly for the past six years.

At the time of examination there was a nonvesicular scaling eruption covering the entire body leaving no free areas. The skin was markedly thickened and lichenized and itched intensely. Scratch, intracutaneous, and passive transfer skin tests have been repeatedly positive to silk. Patch tests were all negative although a large immediate wheal, which faded in a few hours, was obtained to silk protein and silk cloth. Since there was no vesiculation or lasting erythema, the test was judged negative to silk as an agent offending by contact. Hyposensitization to silk was attempted over a period of many months with no benefit to the neurodermatitis although she has had no more asthma. Roentgen ray treatments were of no avail. The trial of various elimination diets over the past two years has not been of any assistance. A course of stock vaccine and at another time an autogenous vaccine from the stool[21] was given but did not help. Autohyposensitization,[30] using blood, was attempted several times but likewise did not help. The child has been hospitalized a number of times and placed in as nearly an inhalant-free room as possible with no benefit.

Urticaria and angioneurotic edema per se are seldom the chief complaint of our children. These conditions most frequently accompany other allergic manifestations and, in our experience, disappear when the chief complaint is successfully treated. Eleven children, however, reported with urticaria as their sole complaint. Seven cases were due to food sensitization; three were not diagnosed; and one was due to feather sensitivity.

Children frequently present urticaria in which the lesions differ radically from the customary wheal we associate with this condition. Starting as ordinary wheals but discrete and comparatively few in number, they become vesicular and then pustular. Since they itch intensely, they have been scratched and are usually raw or covered with a scab when seen. Whether papular urticaria[59] develops because of malnutrition (Sutton, Stelwagon) or because of "extreme susceptibility of the skin in young children" (Holt) or whether it is a transition phase between ordinary urticaria and neurodermatitis (Sulzberger) or is a definite clinical entity, we cannot state at this time.

SUMMARY

1. Asthma due to extrinsic factors, to infection and to both, presents fairly characteristic clinical types each requiring a different approach for successful treatment.

2. Mixed stock vaccines have a real use and give fairly consistent results in properly selected cases of asthma.

3. In order to obtain good results, treatment of allergic manifestations must be given over long periods of time.

4. Various secondary manifestations in allergic children, such as sinusitis, urticaria, or angioneurotic edema, may usually be ignored in the expectation that successful treatment of the chief complaint will rid the child of the secondary conditions.

5. Testing each patient by scratch, intracutaneous, and passive transfer methods is well worth the time consumed even in a busy clinic.

6. The scratch test used alone is not reliable.

7. It is essential to test clinically all allergens giving positive skin reactions before judging them significant.

8. The reactivity of the skin itself varies with the individual and must be taken into consideration in reading reactions.

9. Constitutional reactions to intracutaneous tests need not occur in pediatric allergy practice.

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CELIAC DISEASE

Intestinal Absorption and Gastrointestinal Motility

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CELIAC disease has been an enigma to the pediatrician since its first description by Samuel Gee in 1888. The theories as to cause are nearly as numerous as the number of observers. The disagreement as to cause is, however, offset by a comparative agreement as to symptoms and manifestations.

The generally accepted symptoms are:

1. Great enlargement of the abdomen, in striking contrast to extreme emaciation of extremities and buttocks;
2. Enormous sized stools which are pale and porridge-like, with offensive odor and containing 40 to 80 per cent of the fat digested but unabsorbed;
3. Persistent failure to gain in height and weight (infantilism);
4. Backwardness in speech with precocity in understanding;
5. Flat blood sugar curve after glucose tolerance test meal;
6. Secondary anemia.

Based upon the above recorded symptoms, all research seeking the cause of celiac disease has failed to establish an acceptable conclusion. A notable recognition is made, by all recent workers, in that there is agreement that fats are digested but are poorly absorbed, that carbohydrates are digested and are slowly absorbed, and that proteins are digested and are absorbed. This has established the disease definitely as a disease of disturbed intestinal absorption. Thus it is a disease of malnutrition with periods of steatorrhea when fats reach too high a percentage within the intestine and with periods of fermentative diarrhea when carbohydrates reach too high a percentage. The present-day treatment therefore follows a high protein diet. Haas has added to this the banana to permit a normal carbohydrate diet, assuming that banana, which contains much invert sugar, is more readily absorbed than carbohydrates, which contain little or no invert sugar.

I have recently had two severe cases in which an unusual opportunity for close and continued observation was presented. I present reports of these.

CASE REPORTS

Case 1.—J. B., male, aged two and one-half years, was 32½ inches tall and weighed 21 pounds, 12 ounces on June 6, 1934. He had been healthy until one month previous to my examination when an exhausting diarrhea began without apparent cause, during the period of which there was a weight loss of 5½ pounds.

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Read at a meeting of Region IV of the American Academy of Pediatrics, August 11, 1935.

It had been observed that for several months the stools had been bulky and numbered from two to four daily. All of the classical symptoms of celiac disease were present. The child was placed upon a high protein plus banana diet and an extensive search made for any new symptom or treatment response. It was noted that a diminished intestinal peristalsis was heard and that a nightly weight loss of 2 to 3 pounds occurred, accompanied by a nocturia. The night bed-wetting prevented an accurate urine output measurement, but the parents estimated that two-thirds of the twenty-four-hour urine output was excreted between 7:00 P.M. and 7:00 A.M.

Following the suggestion of Haas, I prescribed castor oil once weekly to rid the bowel of the voluminous foul-odored contents. This succeeded in eliminating the

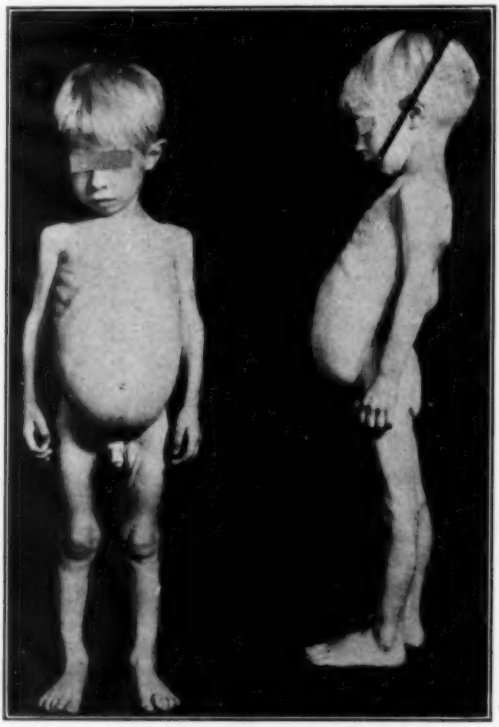

Fig. 1.—Case 1. June 20, 1934. No treatment except high protein plus banana diet.

characteristic celiac odor but, to our surprise, did not act as a laxative. It caused the stool to become formed, the nocturia of the following night to disappear, and the night weight loss to approach the normal. The persistency of this led me to prescribe daily morning doses of cascara sagrada. The effect of this constant intestinal stimulus was:

1. A normal intestinal peristalsis was heard.
2. Approximately two-thirds of the urine output was voided during the day and one-third during the night.
3. The former 2- to 3-pound night weight loss was reduced to from ½ to 1¼ pounds.
4. The blood sugar curve rose to 90-96-130-100.

5. The child had a better appetite and sense of well-being.
6. The stools became formed.
7. Over a period of six months, there was no return to celiac type stools.

Posterior pituitary, to increase intestinal peristalsis, was used for a short time with the same results. During the past year the boy has gained 2 and ⅞ inches in height and 10 pounds in weight.

The clinical impression in this case is that any procedure which increases intestinal peristalsis in celiac disease increases in some way water absorption and elimination and speeds up glucose absorption to the point where a normal blood sugar curve may be found. This impression comes from the observation that most of the water drunk during the day is excreted during the day if intestinal peristalsis is normal, and that the blood sugar curve taken in the absence of an intestinal stimulant is flat but taken in the presence of an intestinal stimulant is normal or nearly so. On March 7, 1935, while the patient was not under the influence of a laxative, the blood sugar curve was 87-94-88-78. On March 26, 1935, while the patient was under the stimulus of cascara sagrada, the blood sugar curve was 90-96-130-100.

Fig. 2.—Case 1. July 26, 1935. After six months of taking a balanced general diet. Treatment: 10 minims fluid extract of cascara sagrada each morning to increase intestinal peristalsis. Weight gain, 10 pounds. Height gain, 3 inches during past year.

The conclusions from these observations led to a more analytical study of Case 2.

CASE 2.—L. S., female, aged six and one-half years, was 38½ inches tall and weighed 22¼ pounds on Jan. 1, 1935. She presented all of the classical symptoms of celiac disease. The history pointed to the onset at the age of one and one-half years, when she had severe diarrhea followed by an obstinate failure in height and weight gain. During the period from one and one-half years to six years the stools were bulky, and the attacks of diarrhea were numerous. The case remained undiagnosed until admitted to the King County Hospital in December, 1934, where

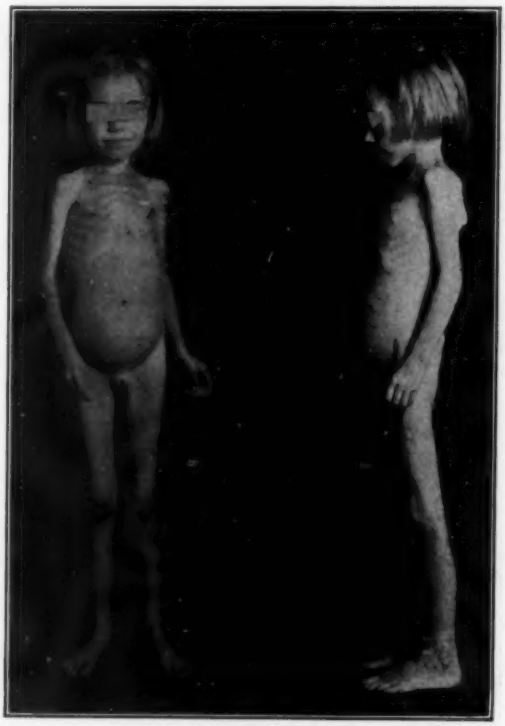

Fig. 3.—Case 2. Dec. 11, 1934. No treatment except high protein plus banana diet.

the girl was placed upon a high protein plus banana diet and referred to my service in the Seattle Children's Orthopedic Hospital.

Upon treatment consisting only of high protein plus banana diet, we found the following accepted symptoms:

1. Infantilism and extreme malnutrition (height 38½ inches, weight 22¼). Enormously enlarged abdomen. Emaciated extremities and buttocks.
2. Four to six large, mushy, offensive stools daily.
3. Obstinate failure to gain height and weight.
4. Backwardness in speech with precocity in understanding.
5. Flat blood sugar curve, 72-74-76-76.
6. Hemoglobin 40 per cent.

In addition, we found:

1. An extremely feeble intestinal peristalsis as observed by auscultation.
2. A night weight loss of 2 to 3 pounds.
3. A low specific gravity of urine (usually 1.008).
4. Barium meal gastrointestinal study revealed one-third of the barium still in the stomach at the end of eight hours, head of barium at the transverse colon after twenty-four hours, no barium passed after forty-eight hours, no picture taken after seventy-two hours, still a large quantity of barium in the sigmoid after ninety-six hours.
5. Approximately two thirds of the total twenty-four-hour urine output was voided between 7:00 P.M. and 7:00 A.M.

Fig. 4.—Case 2. May 5, 1935. After five months of taking a moderately high protein, balanced diet. Treatment: at times 5 minims posterior pituitary twice daily hypodermically, at times 10 minims fluid extract of cascara sagrada each morning to increase intestinal peristalsis. Weight gain, 10 pounds. Height gain, one-half inch. This after four years of stationary weight.

It was decided to give posterior pituitary extract twice daily in doses of 5 minims to increase intestinal peristalsis. After a few days, the following changes took place in the symptomatology:

1. Normal intestinal peristalsis could be heard;
2. Night weight loss decreased;
3. The specific gravity of the urine rose to 1.018;
4. Blood sugar curve rose, 78-98-130-110;
5. Barium meal gastrointestinal study revealed the stomach empty after eight hours, all barium in the colon after twenty-four hours, and all barium passed after forty-eight hours;

6. Approximately one-third of total daily urine output was voided between 7:00 P.M. and 7:00 A.M.;

7. Stools were reduced to one or two daily, well formed and having no characteristic celiac odor;

8. Appetite was good;

9. She had a sense of well-being;

10. She was more active physically;

11. Weight, which had been stationary for six months, increased 4 pounds in the first six days. (See Tables I and II.)

The girl was then given a high calorie general hospital diet for one month and continued to maintain a fairly normal intestinal absorption. Both posterior pituitrin and cascara sagrada were at different times used as intestinal stimulants. She was discharged from the hospital on April 25, 1935, weighing 30½ pounds.

TABLE I

NO TREATMENT EXCEPT HIGH PROTEIN PLUS BANANA DIET

DATE 1935	7 A.M. WT.	7 P.M. WT.	SP. GR.	DAY INTAKE (IN C.C.)	NIGHT INTAKE (IN C.C.)	DAY URINE OUTPUT (IN C.C.)	NIGHT URINE OUTPUT (IN C.C.)
January 14	21¾	23¾	1.006	660	180	135	665
January 15	21¼	23½	1.008	900	180	180	455
January 16	22¼	23¾	1.010	960	180	385	425
January 17	21¾	23¼	1.008	960	210	300	640
January 18	21	24¼	1.010	1050	360	380	490

During the above five days there were observed two to four stools daily; definitely diminished peristalsis; flat blood sugar curve—72-74-74-78; two-thirds urine output passed between 7 P.M. and 7 A.M.; low specific gravity of the urine. Barium meal gastrointestinal x-ray study showed large residue in stomach after 8 hours and large residue in sigmoid after 96 hours.

TABLE II

FIVE MINIMS OF POSTERIOR PITUITARY BID

DATE 1935	7 A.M. WT.	7 P.M. WT.	SP. GR.	DAY INTAKE (IN C.C.)	NIGHT INTAKE (IN C.C.)	DAY URINE OUTPUT (IN C.C.)	NIGHT URINE OUTPUT (IN C.C.)
January 25	23¼	27¼	1.016	990	180	880	500
January 26	25½	28¼	1.016	1240	180	800	520
January 27	25¼	28	1.016	1200	180	880	250
January 28	26¼	29½	1.016	1200	180	800	360
January 29	26¾	29½	1.024	870	180	730	350
January 30	27	29	1.016	1220	180	920	275
January 31	27¼	28¾	1.016	960	180	950	270
February 1	27	28¼	1.012	960	180	950	270
February 2	27	28¾	1.020	840	180	460	180

During the above nine days there were observed active peristalsis; weight gain 4 pounds— blood sugar curve—78-98-130-110. Barium meal study showed stomach empty in 8 hours and gastrointestinal tract free from barium in 48 hours. Urine specific gravity was normal; two-thirds of urine output was passed between 7 A.M. and 7 P.M. Stools were reduced to 1 or 2 daily. She had a better appetite and a sense of well-being.

Another manifestation of altered physiology observed in these two cases is that there was apparently an extreme atony of the urinary bladder. Both children would at times void sixteen or more ounces of urine. A cystogram of the girl was made after the injection of twenty-two ounces of sodium iodide solution. This suggests a possibility of

the cause of celiac disease being ultimately found in a general smooth muscle dystrophy, or a disturbance of innervation of the sympathetic nervous system.

COMMENT

These cases are reported because they presented a syndrome which was spectacularly reversed by the simple expedient of a stimulant to gastrointestinal peristalsis.

Biologic development of the selective lacteal and blood vessel intestinal absorption has evolved in the presence of the normal alternating intestinal movements known as segmentation and peristaltic waves. It may be that any suspension of these muscular contractures results in a lowered circulation in these vessels, and such dilation of the intestinal tract as may follow causes a stretching and narrowing of these vessels to the point where the physiologic functioning of selective absorption is diminished in direct ratio.

This explanation may clarify problems other than celiac disease. This may be the reason why there is no absorption in a distended postoperative intestinal ileus.

By way of hypothesis we may regard normal gastrointestinal absorption as dependent upon normal gastrointestinal motility. In celiac disease gastrointestinal motility has in some way been largely suspended and intestinal absorption of all food elements including fats, carbohydrates, proteins, salts, vitamins, and water has been reduced to the laws of filtration and osmosis, with the result that the accumulated bowel contents distend the intestinal tract and cause the principal diagnostic sign, the large abdomen.

The gastrointestinal tract in this disease then becomes a great reservoir containing enormous quantities of digested food elements, to be absorbed slowly and evenly throughout the twenty-four hours and to await some peristalsis stimulant to cause a period of more rapid absorption, as indicated by blood curves. Upon this basis it would follow that treatment should include an intestinal peristaltic stimulant administered daily to restore physiologic waves of food curves to the blood. It is during these waves that metabolism establishes a reserve storage. As soon as an intestinal stimulant acts as a laxative, it should be discontinued because the bowel has then taken up its former activity and can carry on without aid.

This report is presented with the desire that pediatricians duplicate these experiments in their active cases to determine whether such findings are present in all cases or were present in these as individual peculiarities only. If these findings are present generally, this report may present a new approach to the ultimate solution of a baffling problem. At least, it is hoped that a reduction in emaciation and a shorter period for cure may be effected.

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ENURESIS

A Statistical and Analytical Study

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THE records of 187 cases of enuresis in children and young adults seen at the Philadelphia Child Guidance Clinic were examined to determine the etiologic factors and their significance in enuresis. Sex, age, race, religion, marital status, economic status, nativity, size of the families, intelligence quotient, and reasons for referring the cases were considered. The figures obtained were compared with those of the general clinic intake for all patients. A difference above 5 per cent or more was considered significant. Sixteen of the 187 cases were analyzed under the following headings: (1) past history, (2) physical examination, (3) history of the enuresis, (4) parents' attitudes to the patient, (5) sibling's attitude to the patient, (6) parents' attitudes to each other, (7) parents' attitudes to other siblings, (8) patient's reactions including (a) reaction to parents, (b) reaction to companions, (c) reaction to siblings, (d) reaction to school and school work, (e) history of sex episodes, (f) fears, and (g) neuropathic family history. The treatment of enuresis was not considered in this paper.

The literature of the past ten years on the subject of enuresis abounds with many theories pertaining to the cause of this common condition of childhood and adolescence. Enuresis is considered as a definite disease by some and by others as a symptom of functional or organic disease. The problem of enuresis has been studied by men in many of the branches of medicine and surgery, but especially by the pediatrician, the urologist, and more recently by the psychiatrist. There seems to be a definite trend toward a psychic rather than physical consideration. Many physicains are now sending these patients to child psychiatrists and child guidance clinics. Formerly the frequent practice was to advise circumcision, tonsillectomy, or to prescribe an anthelminthic. Mohr and Waterhouse,[1] Partridge,[2] and Bleyer,[3] found that no definite connection existed between enuresis and specific physical defects.

Campbell,[5] a urologist, made a recent and important contribution to the study of enuresis. He studied 330 cases of enuresis in children over four years of age in whom the usual methods of treatment had failed. He showed that approximately two-thirds of the patients had definite uropathologic changes. He believes that 90 per cent of enuretic patients show no organic condition and that this large group will respond readily to the commonly employed medical and psychotherapeutic measures. Some of the conditions found on cystoscopy in cases of persistent

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Presented in part before the Philadelphia Pediatric Society, November 12, 1935.

enuresis were trigonitis, verumontanitis, neuromuscular disease of the bladder outlet, congenital posterior urethral valves, urethral stricture, vesical stone, and infections of the upper urinary tract including tuberculosis. Campbell did not mention the reversal of urine concentration as a cause of enuresis. Friedell[7] and Batty[4] found a nocturnal reversal of urine concentration in some of the cases studied by them.

Cameron[8] believes enuresis to be a functional disorder and that it should be recognized as a manifestation of hysteria.

Reasons for Referring of Cases to the Clinic.—Examination of the reasons for referring the cases to the clinic (Table I) shows that the patients were referred solely for the enuresis in only fourteen cases. In the remaining cases enuresis was associated with one or more symptoms of a behavioristic nature, namely, stealing, lying, truancy from school, temper tantrums, and stubbornness. Earl[9] reports thirty-eight

TABLE I

SHOWING REASONS FOR REFERRING CASES TO CLINIC

CAUSE	NO. OF TIMES REFERRED
A. For enuresis	14
B. For enuresis plus one or more of the following:	173
1. Stealing	29
2. Truancy from school	16
3. Lying	15
4. Disobedience	14
5. Poor school work	14
6. Temper tantrums	10
7. Masturbation	9
8. Nervousness	9
9. Stubbornness	8
10. Soiling	7
11. Backwardness in school	6
12. Negativism	6
13. Truancy from home	5
14. Fearfulness	4
15. Unsocial attitudes	4
16. Quarrelsomeness	3
17. Crying easily	3
18. Misbehavior in school	2
19. Destructiveness	2
20. Untidiness	2
21. Sex play	2
22. Timidity	2
23. Troublemaking	2
24. Liking to play like a girl	2
25. Jealousy	2
26. Stuttering	2
27. Daydreaming	2
28. Mental retardation	2
29. Slyness	2
30. Night terrors	2
31. Unmanageable	2
32. Irresponsibility	1
33. Epileptic spells	1
34. Fanting spells at confession	1
35. Unpopularity	1
36. Domineering	1
37. Starting fires	1
38. Defiance	1

cases from the London Child Guidance Clinic only four of whom had bed-wetting as their sole symptom. The coexisting disorders were temper (10 cases), lying (9 cases), stealing (7 cases), sensitiveness (6 cases), shyness (5 cases), destructiveness (5 cases), masturbation (4 cases), seclusiveness (3 cases), and sex play (2 cases). He believed that these symptoms were associated with the so-called neuropathic child. He stated, "One clinical fact which emerges is that when one has weeded out the gross physical abnormalities, the psychopaths, and the morons, one is left with a residue, the neuropathic child. And in the neuropathic child certain behavior disorders are common, namely, stealing, lying, truancy, masturbation, temper tantrums, fears, phobias, and bed-wetting."

Ebaugh[10] in his classification of child guidance problems considered many of the above mentioned complaints as protest reactions and placed them under the heading of reactive behavior disorders. He explained that these protest reactions usually develop on the basis of frustrations, disappointment, or antagonism toward others, especially those in authority. Strecker and Ebaugh[11] called this the attacking and counterattacking principle and explained that the child may vigorously resent certain disciplinary measures and may counterattack by running away, exhibiting temper tantrums, or by a general negativism.

Sex.—Two-thirds of the 187 children studied, 121 (64.7 per cent), were males, and one-third, 66 (35.3 per cent), were females. The general clinic intake for all patients was 638 of whom 433 (67.9 per cent) were males and 205 (32.1 per cent) females, a similar proportion of two-thirds and one-third, respectively. The difference was 3.2 per cent in each instance. Anderson[12] and Bleyer[3] found the sexes equally divided, while Batty[4] in his series showed a preponderance of girls over boys with percentages of 56 and 44, respectively.

Race.—Negroes comprised less than one-tenth of the total, there being 14 (8.6 per cent) negroes and 171 (91.4 per cent) white children. This compares closely with the general clinic intake of 31 (6.6 per cent) negroes and 607 (93.4 per cent) white children, with a percentage difference of 2.0 (Table II).

Religion.—The religion was known in 163 of the 187 patients. One-half of the enuretic children were of the Protestant faith, 77 (47.2 per cent), while the Catholic and Hebrew faiths made approximately one-fourth each of the total number, there being 39 (24.0 per cent) Catholics and 44 (27.0 per cent) Hebrews. The clinic intake figures were 305 Protestants (49.8 per cent), 169 (27.6 per cent) Catholics, and 135 (22.1 per cent) Hebrews (Table II).

Economic Status.—The economic status was known in 175 patients. Of this number 50 (28.6 per cent), or approximately one-third, were in the dependent group; one-third were in the marginal group, 56 (32.0 per cent); while the moderate and comfortable groups were each one-

TABLE II

ETIOLOGIC FACTORS STUDIED WITH COMPARISON OF FIGURES OF CLINIC INTAKE*

ETIOLOGIC FACTORS	NO. IN STUDY	PER CENT IN STUDY	PER CENT IN CLINIC INTAKE	NO. IN CLINIC INTAKE	PER CENT DIFFERENCE
Sex:					
Total known	187			638	
Unknown	---			---	
Male	121	64.7	67.9	433	3.2
Female	66	35.3	32.1	205	3.2
Race:					
Total known	185			638	
Unknown	2			---	
White	171	91.4	93.4	607	2.0
Negro	14	8.6	6.6	31	2.0
Religion of family:					
Total known	163			612	
Unknown	24			26	
Protestant	77	47.2	49.8	305	2.6
Catholic	39	24.0	27.6	169	3.6
Hebrew	44	27.0	22.1	135	4.9
Mixed	3	1.8	0.5	3	1.3
Economic status:					
Total known	175			627	
Unknown	12			11	
Dependent	50	28.6	18.2	114	10.5
Marginal	56	32.0	32.7	205	0.6
Moderate	36	20.6	15.9	100	4.8
Comfortable	32	18.2	29.2	183	10.7
Affluent	1	0.6	4.0	25	4.0
Nativity of patients:					
Total known	184			638	
Unknown	3				
American	183	99.5	94.8	616	4.7
Foreign born	1	0.5	5.2	22	4.7
Intelligence quotient:					
Total known	127			617	
Unknown	60			21	
Below 90	48	37.8	36.1	223	1.7
90 to 110	57	44.7	40.2	248	4.5
Above 110	22	17.5	23.7	146	6.2

*Percentages calculated in terms of total number of cases known.

fifth of the total, there being 36 (20.6 per cent) and 32 (18.2 per cent) respectively. The family of only one patient was affluent. Two-thirds of the families of enuretic children are therefore in poor financial circumstances. This fact becomes more apparent when these figures are compared with those of the similar groups in the general clinic intake. In the latter the status was known in 627 of the 638 cases. The dependent and marginal groups comprised over one-half of the total number, the figures being 114 (18.2 per cent) and 205 (32.7 per cent), respectively. The percentage difference between the families of enuretic children and the general clinic intake of dependent families was 10.5 per cent higher in the former. Conversely, in the comfortably situated

group, the families of enuretic children were fewer by 10.7 per cent, showing, therefore, that the economic status is significant in enuresis (Table II).

Intelligence Quotient.—The intelligence quotient was determined in 127 patients. Of these, over one-third, 48 (37.8 per cent), were below 90. Fifty-seven (44.7 per cent) were between 90 and 110, and 22 (17.5 per cent) were above 110. In the general clinic intake the intelligence quotient was known in 617 cases. Here, too, over one-third were below 90, there being 223 (36.1 per cent) cases; 248 (40.2 per cent) were between 90 and 110; and 146 were above 110 (Table II).

Nativity.—The birthplace of the patient was known in 184 cases. Only one child was of foreign birth. The clinic intake showed that 616 patients (94.8 per cent) were born in this country and 22 (5.2 per cent) were of foreign birth (Table II).

Marital Status.—The marital status of the parents was known in 175 cases of enuretic children and in 632 of the clinic intake of patients, there being no data in 12 of the former and 6 of the latter group. The parents of enuretic children were found to be living together in two-thirds, or 121 (69.1 per cent), of the cases. In the general clinic intake parents in 337, or approximately one-half (53.3 per cent), of the families were living together. The families in which parents were not living together totaled 295 (46.7 per cent). The percentage difference between families of enuretic children and families in the clinic intake was 15.8 in each instance (Table V). The husbands and wives in 54 families of enuretic children were not living together; in 28 this was due to the death of a parent; in 10 the parents were divorced; and in 2 the father had deserted. The parents of 3 patients were unmarried and not living together. No data were obtained as to the cause of the separation in 11 of the 54 families.

Size of Families.—The patient was an only child in one-seventh or 28 (14.9 per cent) of the 187 cases studied (Table III). In the clinic intake of 546 known cases, 103, or one-fifth (18.9 per cent), of the families had an only child, the percentage difference being 4. Families of enuretic children with one sibling constituted one-fourth of the total

TABLE III

SHOWING NUMBER OF SIBLINGS IN FAMILIES STUDIED

SIBLINGS	NO. IN STUDY	PER CENT IN STUDY	PER CENT CLINIC INTAKE	NO. IN CLINIC INTAKE	PER CENT OF DIFFERENCE
0 (only child)	28	14.9	18.9	103	4.0
1	46	24.6	26.6	145	2.0
2	34	18.2	18.9	104	0.7
3 or more	79	42.3	35.6	194	8.7
Total known	187	100.0	100.0	546	--
Unknown	--	--	--	92	--

number of cases, 46 (24.6 per cent) out of 187 cases. The general clinic intake for this group was also one-fourth of the total intake, or 145 (26.6 per cent) cases. The percentage difference was 2. In the enuretic group families of two siblings constituted approximately one-sixth of the total, 34 (18.2 per cent), while in the clinic intake they constituted one-fifth of the total, or 104 (18.9 per cent). The percentage difference was 0.7. Families of three or more siblings constituted approximately two-fifths of the total, or 79 (42.3 per cent), while in the general clinic intake there were 194 (35.6 per cent), or one-third of the total. The percentage difference was 8.7.

Age.—The age range of patients studied was between four and eighteen years (Table IV). The greatest number of children, 27 (14.4 per cent), having enuresis were nine years old. Second highest group was the six-year-old group with 23 children (12.3 per cent), and third

TABLE IV

SHOWING AGE OF PATIENTS STUDIED

AGE IN YR.	NO. IN STUDY	PER CENT IN STUDY	PER CENT CLINIC INTAKE	NO. IN CLINIC INTAKE	PER CENT OF DIFFERENCE
3 or less	0	0	1.3	8	1.3
4	5	2.7	4.2	27	1.5
5	10	5.3	4.5	29	3.8
6	23	12.3	4.5	29	7.8
7	19	10.2	9.1	58	1.1
8	20	10.7	7.5	48	3.2
9	27	14.4	9.4	60	5.0
10	14	7.5	9.4	60	1.9
11	12	6.4	12.2	78	5.8
12	18	9.6	9.9	63	0.3
13	8	4.3	8.8	56	4.5
14	17	9.1	10.5	67	1.4
15	10	5.3	5.5	35	0.2
16	2	1.1	1.9	12	0.8
17 or over	2	1.1	1.3	9	0.2
Total known	187	100.0	100.0	638	--

TABLE V

SHOWING MARITAL STATUS OF FAMILIES OF ENURETIC CHILDREN

MARITAL STATUS	NO. IN STUDY	PER CENT IN STUDY	PER CENT CLINIC INTAKE	NO. IN CLINIC INTAKE	PER CENT OF DIFFERENCE
Total known	175			632	
Unknown	12			6	
Parents living together	121	69.1	53.3	337	15.8
Parents not living together	54	30.9	46.7	295	15.8

Of the parents not living together:

28 cases due to death of a parent
10 cases due to divorce
2 cases due to desertion
3 cases parents were unmarried
11 cases unknown

highest was the eight-year-old group with 20 children (10.7 per cent). The percentage differences when compared with clinic intake figures were 5.0, 7.8, and 3.2, respectively. In the eleven-year-old group the difference was 5.8 per cent, this being higher on the side of the clinic intake.

ANALYSIS OF SIXTEEN CASES

Past History.—The past history in almost every case showed the usual diseases of childhood.

Physical Examination—Physical defects included diseased tonsils and adenoids, dental caries, otitis media, and malnutrition. In one case the patient had a mild scoliosis for which she wore a brace. Urinalyses were negative in all of the patients.

History of Enuresis.—Ten of the 16 patients had enuresis since infancy; in the remaining 6 it started in childhood. Eleven cases were of the nocturnal type and 5 were of combined nocturnal and diurnal enuresis. Enuresis followed attacks of childhood diseases in 2 patients.

CASE 3.—E. D., a white female, aged seven years, the youngest of three children, was referred to the clinic for enuresis. The physical examination and developmental history were negative. The patient developed nocturnal and diurnal enuresis following an attack of whooping cough at the age of four years. Previous medical treatment did not cure the condition and the child was brought to the Child Guidance Clinic. The mother had severely whipped the child, had shamed her in front of visitors, threatened her with diapers, limited the child's fluids, and awakened her at night in an attempt to cure the bed-wetting. The father favored his oldest son. The parents had many quarrels, and their outside interests frequently kept them away from the home. The patient disliked her oldest brother who teased her and treated her cruelly.

Discussion.—In the case of the seven-year-old girl presented, the enuresis dated from an attack of whooping cough. The parents were in discord and had many outside interests. The mother's method of handling the enuresis by shaming the child and scolding her encouraged rather than cured the enuresis. Although the enuresis followed an attack of whooping cough, it may not have been the cause since it is not known what emotional factors occurred at that time.

The parents' methods of handling the problem of enuresis in all our cases were bad. The children were whipped, often severely, shamed before visitors, and threatened. In this case the mother threatened the patient with diapers. In another case the mother attempted to cure the patient of wetting by stuffing the wet part of his trousers into his mouth. The parents in some cases attempted to limit the fluid intake, to awaken the patient at night, and to offer rewards, but these means were not effective. Obviously in patients with marked emotional disturbances and undesirable environmental conditions, treatment intended to improve poor habit training will not cure the patient unless the other untoward factors are removed.

Attitude of Parents to Patient.—In studying the various cases, the attitudes of the parents to the patients were found to be an influence in

causing enuresis. Frequently parents differ in their feeling toward a child. One parent may hate a certain child, and the other may love the child. Often this feeling of hate is due to jealousy. In Case 4 the mother compared the patient unfavorably with the other children; this comparison gave the child a sense of insecurity in the home. In Case 16, the patient, a boy of twelve years, was referred to the clinic for enuresis, stealing, and lying. The father was fearful that he would be discredited by the boy, and his feeling toward him is well illustrated when he told the school principal that the boy "was no good." In Case 12 the father was disinterested and the mother overprotective. The father lost interest in the boy, because since his birth the mother had showered all her affections on the child. She was overprotective for fear that, if the boy was allowed to play with others, he would learn things sexual in nature that she felt he should not know. She has thus prevented his normal social contacts. His stubbornness and disobedience at home and in school may be considered as a protest reaction against his mother. In Case 9 the mother's attitude to the patient was shown definitely to be one of rejection. The mother identified the patient (a girl) with a maternal aunt whom she disliked. She often stated that everything would be right if the patient belonged to the aunt and if the aunt's son was her child. The mother admitted that the patient was not wanted at birth and that she had been an obstacle in some ways. The mother also stated that the child was "dumb" and would not study unless forced to do so. (Although the child had an I. Q. of 92, denoting low average intelligence, her poor school work was partly and directly attributable to the mother, who refused to allow the patient to do her own work.) Instead of allowing the child to develop self-dependence, the mother was forcing her to be dependent upon her, which attitude in itself is faulty hygiene.

There was an only child in seven families. In families in which there was one sister among several brothers, the female was often subjected to much criticism, not only from her brothers, but from the parents as well. In Case 5, the patient was unhappy at home because her poor school work caused much criticism from her brothers and sisters who called her "dumb" and teased her incessantly. Her oldest brother whipped her rather severely when he thought the occasion demanded it—this without any interference from the father. Following a change of teachers, the child did better work; the criticism at home was less, and the enuresis improved markedly.

Stepparents and stepchildren frequently are the cause of much unhappiness to the other children in a household. This often results in protest reactions: thus, the case of one boy who was referred to the clinic for wetting and stealing was cleared up following the death of the stepmother.

Parents' Attitudes to Each Other.—The parents' attitudes to each other were found to be significant in causing enuresis, inasmuch as un-

happy marital conditions have caused in the children emotional disturbances leading to enuresis. In only 3 of the 16 cases were the parents found to be living together in harmonious relationship. There were 2 cases (1 and 12) in which the husbands left their wives because of nagging. In each case, however, reconciliation occurred. In one instance the father had married the mother after a four-week courtship. The husband left his wife for another woman after living together for four years. He charged his wife with nagging. The wife's attitude toward her husband was influenced greatly by her parents, who did not like him. In Case 9 the husband said that he had a good wife. The wife, however, felt that her husband was a weak type of individual. She seemed to "take her husband for granted." She had been accused of "trying to wear the pants in the family." She stated that because of financial reverses her husband had lost confidence in himself. She thought, however, that "he didn't have much to begin with."

Attitude of Parents to Other Siblings.—The attitude of the parents to other siblings in the family was also found to be of significance in our study of enuresis. For example, the positions of the oldest child and of the baby of the family are unique. Many times there seems to be a closer relationship between the first-born and the parents. Too, as long as a child remains the baby of the family much affection is showered upon him. With the coming of the next child, or the growing up of the baby, that affection may lessen. Children are often conscious of the partiality shown other members of the family. This tends to cause a feeling of insecurity in the home on the part of such children. Enuresis will often result from such a situation. In Case 8 the patient, a girl twelve years old, was her father's favorite until the coming of a new child with whom the patient had to share her father's affection. The mother, in addition, had rejected the patient for the oldest son, who became a substitute for the husband she did not understand. This rejection and substitution was shown by the mother when she stated that the patient had always been a disturbing influence in the home in contrast to her son who should have been the girl. She stated that she had lived with her husband for seventeen years and did not feel as though she knew him yet.

Patient's Reactions.—a. *Reaction to Parents:* A study of the reaction of the patient to the parents revealed that in most cases the attachment was closer between parents and children of the opposite sex than between those of the same sex. Some of the patients feared their parents because of the whippings administered. In Case 4 the patient, a girl of nine, complained, "My mother always nags me and never has a good word for me."

b. *Reaction to Siblings:* The reaction of the patient to the siblings was in most cases that of fear, hate, and jealousy. In Case 5 the patient,

a nine-year-old girl, feared her oldest brother because he whipped her and disliked her sister who, she claimed, "picked on her."

c. *Patient's Reaction to Companions:* In two cases the patients had no companions because they lived among children whom the mothers considered unfit company.

d. *Patient's Reaction to School and School Work:* The reactions of the patients to school and their school work were as follows: Four patients were reported as doing fair work and getting along well. Four were reported as being interested. In one case the patient's work improved after a change of teachers, while in another a change from parochial to public school improved the child's work.

It was interesting to note that two personality groups were differentiated after a study of the reactions of these patients to school work, and each bore a close relationship to the type of enuresis. The patient who had enuresis since infancy fell into a group characterized by passivity. In this group could be placed the child who was disinterested in his work, who was doing only passing work, whom the teachers characterized as lazy, inattentive, and unresponsive—the so-called "good child." A principal in describing a child of this group said, "Her conduct is exemplary because she has not the spunk to do anything wrong."

The second group, those who developed enuresis in childhood, includes the aggressive, hyperactive child; the mischief-maker, the child who is disobedient and reacts by temper tantrums or by running away from school.

Sex Knowledge.—Two patients were recorded as being sex curious, two were said to have had sex episodes, and two admitted masturbation.

Fears.—Nine patients out of the 16 studied had fears. Four of the 9 were afraid of the dark; 1 child was afraid of negroes; 1 was afraid of fire engines; and 1 was afraid of his father. Also, 2 were afraid of being kidnapped.

Neuropathic Family History.—The father of one patient was an alcoholic (Case 15). The paternal grandfather was an alcoholic (Case 14), and the maternal aunts and uncles were of low standards.

SUMMARY AND CONCLUSIONS

1. A review of the literature together with a study of the cases reported here suggests that organic disease is not the cause of enuresis except in patients with persistent enuresis in whom definite lesions of the genitourinary tract are found.

2. Sex, race, religion, and nativity of the patients were not found to be significant etiologic factors in enuresis.

3. The economic status of the families of enuretic children is important since enuresis occurred more frequently in children from families of poor financial circumstances.

4. The tendency for enuresis to occur more frequently in children of lower intelligence is noted.

5. A study of the 16 cases showed that marital discord was an important factor in causing unhappiness among enuretic children. The marital status of the families of these children would seem to be good if one considers as a criterion the fact that only a small percentage of them were not living together. However, this does not tell one how much discord is present.

6. Enuresis was found to occur most frequently in the age group between six and nine years and in families of three or more siblings.

7. Childhood diseases as a factor in producing enuresis must be considered in relation to the emotional disturbance arising incident to the illness. This needs further study.

8. Children with enuresis are in the majority of cases trained improperly by their parents who by their improper methods serve only to cause the enuresis to continue.

9. Parental rejection must be considered important in its relation to enuresis. It is amazing how children at a very early age sense this attitude of the parents.

10. Stepparents and their children often cause an unhappy situation for the other children and are indirectly contributory factors.

11. Children with enuresis in most cases are obsessed by fears. The incidence of fear indicates that these children are suffering from a neurosis.

12. Two personality groups may be differentiated depending upon whether the enuresis has continued from infancy or began in childhood. The children of the first group are characterized by passivity, while in the latter group the children are characterized by hyperactivity and aggressiveness.

13. Parental overprotection by preventing the child from becoming independent is an important factor since it leads to the production of protest reactions.

14. Enuresis occurred in association with other complaints of a behavioristic nature, such as stealing, lying, and temper tantrums, more frequently than as the only symptom. If the above complaints are to be considered as protest reactions, then enuresis may also be in the nature of a protest reaction.

This association, also, indicates that the child is suffering from a far more serious condition than bed-wetting because he shows maladjustment not only in his physiologic but in his social life as well.

15. Further studies of the type embodied in this paper need not be made, but the significant points discussed should be studied further. These include economic status, age incidence, intelligence rating, and enuresis following physical illness.

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PAROXYSMAL SNEEZING IN WHOOPING COUGH

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ALTHOUGH whooping cough is one of the most common contagious diseases seen in infants and children, the appearance of sneezing in place of coughing is apparently quite rare. In 1813[1] Watt first reported that whooping cough could appear without a cough and be replaced by coryzal symptoms. Since then several authors have reported this interesting phenomenon. Roger,[2] in a discussion of pertussis in 1883, described two children, one twenty-one months old and the other also young, in whom paroxysmal sneezing occurred intermittently with typical paroxysms of coughing. Szegö[3] in 1900 published the first paper on this subject, describing a case in a child three years old, in whom he noted a laryngospastic stage associated with attacks of sneezing, but without cough. In this case up to ten sneezes were counted in the expiratory phase, with a maximum of twenty-two attacks in twenty-four hours. Henoch[4] in 1903 reported a similar experience with a two-year-old child, in whom the onset and end of the disease were characterized by attacks of paroxysmal sneezing. Meyer and Burghard[5] reviewed 1,064 cases of pertussis in 1925 and noted that this type of sneezing was occasionally seen both at the onset of the disease and in place of the cough at later stages. In 1929 Reichle[6] made careful observations of two cases seen at the Babies and Childrens Hospital in Cleveland. One patient was twenty months old, the other two months old. In the first case, in the third week the child was coughing, sneezing, and vomiting. Typical attacks of sneezing were elicited by touching the pharyngeal wall. Another child in the family had an ordinary attack of whooping cough at the same time. His second patient had sneezing attacks interspersed with paroxysms of coughing. Moncrieff and Lightwood[7] in 1929 reported a case in a girl aged three years and eleven months. This child had typical paroxysms of coughing for three weeks, which were supplanted by attacks of sneezing for the next two weeks. Following this the cough recurred.

REPORT OF CASES

CASE 1.—D. R., female, aged twenty-three months, was seen in clinic, with the complaint of running nose and sneezing of three weeks' duration. During the previous week the sneezing had been of such a violent character that the mother was alarmed. During the examination, an attack was brought on as a result of crying. It consisted of a series of eight to ten sneezes rising in rapid succession to a crescendo. Toward the end of the attack she became extremely cyanotic and expelled a large amount of thick tenacious mucus from the anterior nares. No whoop occurred. Following this she was exhausted. These attacks numbered from ten to fifteen in twenty-four hours. These lasted for three weeks and were then entirely supplanted by attacks of coughing and whooping, which lasted for three more weeks.

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A blood count at the time she was first seen showed W.B.C., 19,000; lymphocytes, 74 per cent; polymorphonuclears, 14 per cent; and monocytes, 2 per cent.

CASE 2.—R. R., female, aged eighteen months, was seen having an attack of paroxysmal sneezing in the elevator of the Mandel Clinic Building on her way to the pediatric clinic. Three weeks previously she had begun having a nasal discharge and a cough. The cough became paroxysmal, and whooping and vomiting occurred. In the third week the attacks of sneezing started. They usually followed a coughing spell. There were from five to seven attacks during twenty-four hours, with about twice that number of coughing spells. The sneezing lasted three weeks, after which coughing persisted for some time. An older sister had whooping cough at the same time with typical symptoms.

PHYSIOLOGY

There is relatively little difference in the mechanism of the respiratory reflexes of coughing and sneezing. Winton and Bayliss[8] state that a cough results from irritation of the mucous membrane of the pharynx and upper end of the trachea and consists of a strong forced expiration, the glottis being closed at the beginning and opened suddenly about halfway through, permitting a violent blast of air to be drawn through the upper respiratory passages. A sneeze, on the other hand, results from irritation of the nasal mucous membranes and consists of a sudden strong forced expiration, during which the glottis remains open, but the communication between the pharynx and the mouth is closed by a contraction of the anterior fauces, so that the air from the lungs is driven through the nose.

COMMENT

The occurrence of the phenomenon of sneezing taking the place of coughing in pertussis is so characteristic that the diagnosis of the disease may be made instantly. As Reichle[6] states, "The sneezing attacks in their staccato repetition, their insistency, and their resulting exhaustion are so strongly reminiscent of the paroxysm of whooping cough, that once such a case has been seen, the symptoms will not be missed again."

Severe sneezing may occur in allergic individuals, but while their attacks may be paroxysmal, cyanosis and exhaustion do not take place. Foreign bodies in the nose may also cause severe sneezing.

Seitz[9] observed that this condition occurs only in young children, and all cases reported to date show that this is true. The attacks of sneezing may be associated with attacks of coughing, or take the place of the cough at any stage of the disease.

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1525 EAST 53RD STREET.

SUMMER TETANY AND THE SERUM CALCIUM

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DURING the height of the summer of 1935 (July and early August) when there was practically no interruption of sunshine by rain, clouds or smoke, two full-blooded negro infants were admitted into the hospital because of recent repeated convulsions. Some evidences of rickets suggested the possibility of tetany, and for these reasons calcium and phosphorus determinations were run as checks to the treatment.

CASE 1.—W. S., a negro boy, aged seven months, was first seen at the hospital July 13, suffering from "spasms" and fever, both of which had been going on for eleven days. The weight at birth had been 5½ pounds, and he had gained 8 pounds since, on artificial feeding alone, evaporated milk, syrup, and water. The administration of cod liver oil had been irregular. The mother is a tall, thin, undernourished but rapidly growing child of thirteen years, who during pregnancy must have had even more demand for calcium because of her age. The infant had a definite rosary; the fontanel was larger than normal; the wrists were thick; and the abdomen was large. The roentgen films confirmed the diagnosis of rickets (Fig. 1).

The determinations of the concentration of the serum calcium show a range from 7.2 mg. on July 15, to 6.4 mg. on July 30, and to 10.1 mg. on August 10; the phosphorus, from 2.8 mg. on July 15 to 4.7 mg. on August 10 (Fig. 3). There was therefore a constant rise of phosphorus from the rachitic zone to the normal level in about four weeks' treatment, consisting of a complete milk formula, 6 gm. of dicalcium phosphate by mouth daily, cod liver oil three times daily, and ultraviolet irradiation daily. No convulsions occurred after the beginning of hospital treatment. The calcium content of the serum was not raised until beginning the use of a calcium salt in the vein. One gram was given in solution, and repeated once, five days later. Within eleven days after injection of first intravenous calcium the elevation to 10 mg. was reached. One month later an even higher figure was reached.

CASE 2.—M. T., negro girl, seven months old, was admitted July 31 because of six "spasms" in the previous two weeks. She had been breast fed entirely for six months and for one month had been given cow's milk, but never any cod liver oil. She had gained 9 pounds since her birth, which was normal.

The serum calcium level was the lowest we have encountered, 4.9 mg., while the phosphorus was always normal. Roentgen ray films showed rickets with some healing (Fig. 2).

The treatment was similar to that of Case 1. During the eight days in which two intravenous injections of a calcium salt were given, the level rose from 4.9 mg. to 10.7 mg. and remained normal on subsequent examinations.

DISCUSSION

Neither of these infants had positive Chvostek or Trousseau signs, laryngospasm, or carpopedal spasm during our observation; and, of course, these are not necessary for a diagnosis of tetany when rickets, the onset of convulsions, and proved low serum calcium level are all present.[1]

From the Department of Pediatrics, School of Medicine, University of Kansas.

The calcium and phosphorus levels were both low at the same time in the first case, possibly as a result of some variation in the mineral balance of the diet at the time.[2]

The factors which explain the development of tetany in the summer in these infants are, first, the deeply pigmented skin, the susceptible age

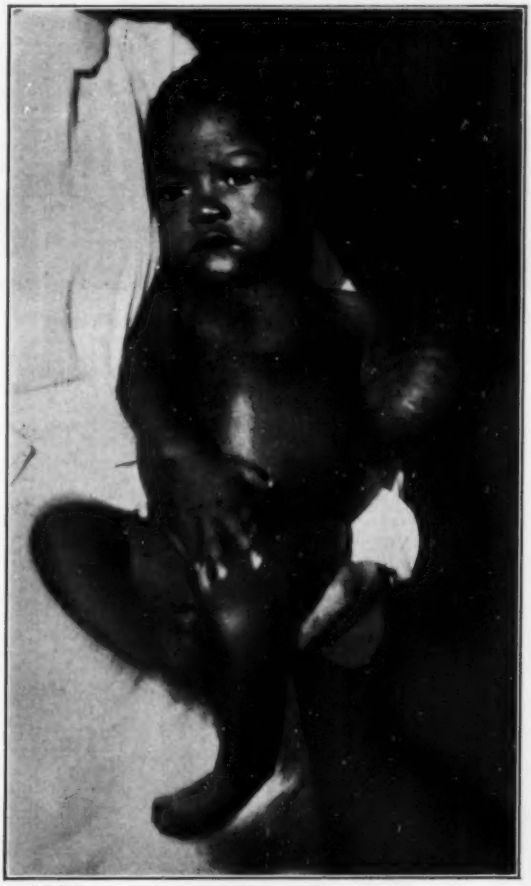

Fig. 1.—W. S., August 2, 1935. This photograph shows the thickened wrist and the pot belly. The child voluntarily curved the foot at this moment, carpopedal spasm being absent.

in infancy, the presence of untreated rickets the previous winter, and incompletely cured rickets during the short period in March when there was about the usual amount of sunshine. Then came the period of exceptionally rainy and cloudy days in April, May, and June.[3] Infants during this period were kept indoors because of rain; they were more completely covered with clothes than usually at this time of year.[4]

Our dispensary and hospital records for the past ten years contain no cases of tetany during the summer months. Writers upon the subject omit the mention of calcium determinations at that time of year.

Fig. 2.—M. T. Widened and frayed ends of the tibiae at the ankles, with the appearance of some healing.

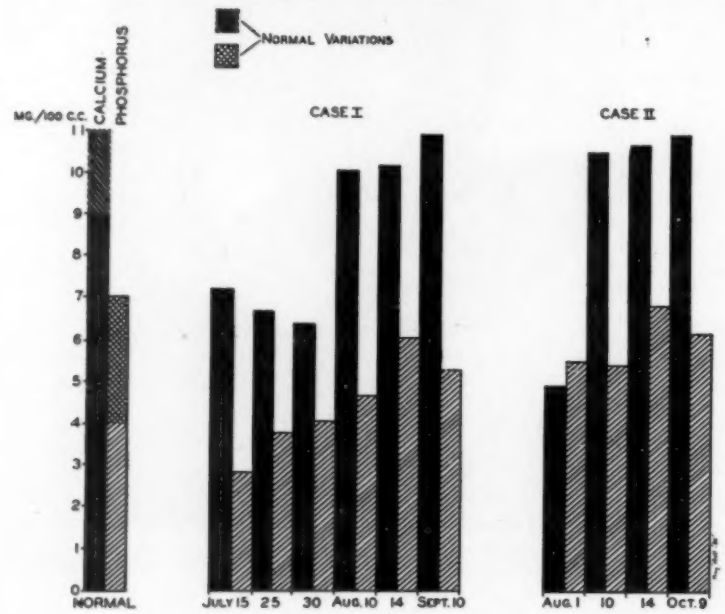

Fig. 3.—Calcium and phosphorus levels.

György states that tetany in summer occurs only sporadically and then rarely. It is known, however, that rats have developed rickets in the open air even during the summer, when the sunshine of the manufacturing city has been steadily obscured by smoke.

This year the period of interruption of exposure to sufficient sunlight was at least sixty days, which agrees with the experimental findings reported by Gerstenberger. That the amount of ionized calcium in the circulating blood is low because of an incomplete diet and the supply depleted during this period of inadequate exposure to sunlight by the withdrawal into the bones of the healing rickets seems a logical conclusion as to the production of tetany in these infants.

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914 Medical Arts Building

MULTIPLE HEMANGIO-ENDOTHELIOMAS OF THE LIVER

Report of a Case

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OF THE many abdominal tumors occurring in infancy, multiple hemangiomas of the liver, more properly termed hemangio-endotheliomas, are among the rarest. A complete review of the literature on this subject was given by Kunstadter[1] in 1933. He included an analysis of fourteen previously reported cases and added a fifteenth one personally observed. The purpose of this presentation is to record an additional case in which this condition was present.

History.—C. W. F., a white female, three months old, came under observation on Aug. 6, 1935, because of an enlarged abdomen and obstinate constipation.

The infant was delivered by forceps three weeks prematurely. The birth weight was 6½ pounds. The abdomen had been protuberant and "fat" since birth, but no particular attention had been paid to it. She was breast fed, but vomited frequently after feedings. About two weeks prior to coming under observation, she began to have obstinate constipation. Bowel evacuations could be effected only with enemas. On August 4, the abdomen seemed distended and rigid, much more so than usual, according to the mother. Enemas and pills failed to induce an evacuation. The patient was then brought to the hospital.

Physical Examination.—The patient was well nourished and well developed, weighing 6,625 gm. The temperature was 99.6° F. rectally. The only external marking present was a small elevated hemangioma in the skin, 7 cm. below the right nipple.

The head, eyes, ears, nose, and throat were normal. Palpation of the cervical region revealed no lymphadenopathy.

The circumference of the chest was 38 cm. at the nipples. The lungs were clear and the heart apparently normal.

The abdomen was protuberant, firm and rigid, especially in the upper portion. Mensuration revealed the abdomen to have a circumference of 48 cm. at the umbilicus, and 5 cm. above this point a circumference of 49 centimeters. A mass could be felt in the upper portion of the abdomen extending downward to within 2 cm. of the umbilicus. It apparently filled the entire upper right quadrant and extended about 6 cm. to the left of the midline. The edge of the tumor mass could not definitely be palpated. Percussion revealed a dull note over the entire mass, the remainder of the abdomen being tympanitic. Auscultation gave no further information.

The extremities and genitals showed no abnormalities.

Laboratory Findings.—Urine was normal.

Blood: Hemoglobin (Sahli) 44 per cent; red blood cells, 2,290,000; white blood cells, 9,000; differential—neutrophiles, 18 per cent; eosinophiles, 2 per cent; lymphocytes, 62 per cent; endothelial cells, 18 per cent.

Blood Wassermann and Kahn tests were negative.

Agglutinations for members of the typhoid-colon-dysentery group were negative.

The blood calcium content was 9.5 mg. per cent; phosphorus, 7 mg. per cent; icterus index, 4.

From the Department of Pediatrics, College of Medicine, State University of Iowa.

The van den Bergh test showed a biphasic reaction, and qualitatively was negative.

The arm band test was negative.

The bleeding time: Capillary, 4 minutes; venous, 4 minutes.

Fragility of red cells ranged from 0.44 per cent to 0.32 per cent.

Clot retractility 4 plus in 4 hr.

Platelets, 0.4 per cent.

Hematocrit, 24 per cent.

Hemoglobin (Newcomer), 5 gm.

Reticulocytes, 2.2 per cent.

A *roentgenogram* revealed a mass resembling liver in the upper abdomen, with displacement of the intestines downward.

The tentative diagnoses were (1) malignant tumor of the liver; (2) malignant tumor of the kidney or adrenals; and (3) retroperitoneal tumor.

Fig. 1.—Roentgenogram of abdomen, showing a large mass occupying the upper two-thirds of the abdomen, with downward displacement of the intestines.

Attention was called to the hemangioma in the skin, and a casual comment made that the hepatic tumor might possibly be of the same nature.

By intravenous pyelography both kidneys were visualized normally. The abdominal mass was definitely above these organs.

The patient had an irregular temperature ranging from 98.6 to 102° F. rectally. She had frequent small emeses. It proved necessary to give one enema on the second day of observation, after which the infant spontaneously passed three to eight soft yellow stools daily.

On August 11, at 8:30 P.M., the infant suddenly became cyanotic and dyspneic. There was much mucus in the throat, and numerous fine râles could be heard throughout the chest. Oxygen and suction failed to give relief. Adrenalin administered intramuscularly was without avail. She became progressively worse and died within half an hour. The clinical diagnoses were pulmonary edema and malignant tumor of the liver.

Necropsy Findings (Summarized by Dr. R. E. Shaw).—External examination showed only the findings already given.

Fig. 2.—Liver after Pick's fixation. Superior surface.

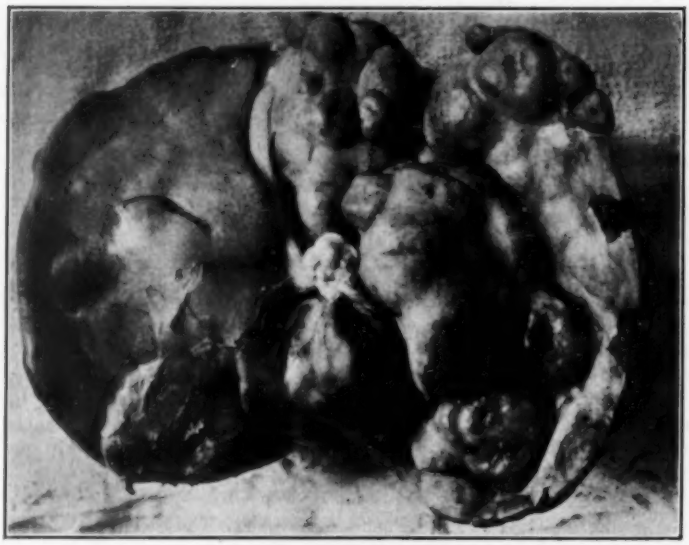

Fig. 3.—Liver after Pick's fixation. Inferior surface.

The serous cavities contained no free fluid and no adhesions. The lungs showed pulmonary edema and beginning bronchopneumonia in the posterior portions—findings which were confirmed microscopically. The liver was enormously enlarged

and had displaced the intestines downward. The surface of the organ was everywhere studded with large, fluctuant, purple blebs, which were thin walled and filled with blood. On section there were seen a multitude of nodules which were apparently separate from each other. The majority were round, but many were lobulated. In general the nodules were dark red in color, but peripherally each nodule faded into a pearl gray zone, and throughout the central portion of each could be seen a fine, lacelike pattern of gray strands in which the blood was held. The liver tissue in between the nodules was of a light brownish color. Microscopically the tumor nodules were found to be made up of irregular, blood-filled, vascular spaces. These spaces were separated by connective tissue strands supporting a single layer of thickened endothelial cells. In the peripheral portion of each tumor the vascular spaces were smaller and the amount of connective tissue less. Endothelial cells were found to be clumped in places, and occasionally to be invading the liver substance, but for the most part each tumor had a false capsule of compressed atrophic liver tissue.

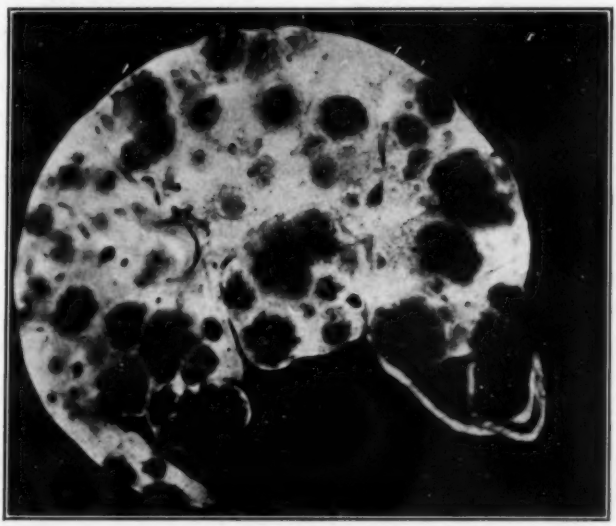

Fig. 4.—Horizontal section of liver after Pick's fixation. This shows the amount of liver tissue replaced by the hemangiomas.

The intestinal tract appeared normal except for one small, soft, reddish nodule in the descending colon. The microscope showed that this tumor nodule lay in the mucosa and submucosa. It had the same histologic appearance as the tumor nodules of the liver, with the exception that the vascular spaces were smaller. The overlying epithelium was intact. A small reddish tumor nodule from the skin of the upper abdomen showed a similar picture histologically. It was rather cellular but had definite blood-filled spaces. Demarcation from the surrounding tissue was rather poor.

No hemangiomatous nodules were found in other organs.

DISCUSSION

While the diagnosis of a tumor of the liver could be made clinically with a fair degree of certainty, there were marked difficulties encountered in trying to make a more specific diagnosis.

Kunstadter has attempted to correlate the clinical findings in fifteen cases of hemangio-endotheliomas of the liver in order to emphasize certain features which should bring this uncommon condition to mind. He cites the presence of an enlarged abdomen since birth, the various gastrointestinal disturbances (vomiting, constipation, and abnormal stools), progressive course, and respiratory embarrassment as common to these patients. However, all these symptoms are present to a greater or less extent in association with many abdominal tumors.

There are two features in this patient's findings which might have led to a correct diagnosis. The first of these is the presence of the skin hemangioma. Such a finding has been reported twice previously, by Brüchanow[2] and Orzechowski,[3] the latter's patient having multiple skin lesions of this type. Available data seem to justify the view that hemangio-endotheliomas present since birth may be considered as congenital defects or anomalies of the vascular system. It is therefore logical to suppose that the hemangiomas will not necessarily be confined to any one location. Rather than to consider these tumors as malignant with invasive qualities, we might well classify them as multiple tissue defects which, because of their size and location, cause damaging pressure effects. Five of the cases reviewed by Kunstadter showed hemangiomas in other locations, including spine, ribs, lymph nodes, skin, and lungs. The variability of their location makes the theory of metastasis seem unlikely and unnecessary. The presence of a hemangioma of the skin, or a demonstrable one in any other portion of the body, in the presence of a hepatic tumor, should suggest the possibility of multiple hemangio-endotheliomas of the liver.

The second significant finding is in the blood picture. The hemoglobin content was 44 per cent with 2,290,000 red cells and 2.2 per cent reticulocytes. There was no cachexia or other stigma of malignancy. That the anemia was not nutritional in origin is borne out by the fact that the color index was normal and the hematocrit reading was low (24 per cent). The large volume of viscid blood contained within the liver may explain the anemia on the basis of compensatory dilution to maintain blood volume.

SUMMARY

A case record of multiple hemangio-endotheliomas of the liver is presented, including complete necropsy findings. The pathology present was in all respects similar to that previously reported by others. Hemangiomas of the skin and certain characteristics of the blood picture were stressed as possible aids in establishing the diagnosis.

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EVENTRATION OF THE DIAPHRAGM

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EVENTRATION of the diaphragm is a rare anomaly, best defined as an elevation of this structure permitting some of the abdominal contents to occupy the space normally containing the thoracic organs. The term "eventration" is misleading as it implies an escape of viscera from the abdominal cavity, suggesting an opening in the diaphragm. Such is not the case, since the diaphragm, although thinned out, is intact. This designation should be abolished and "elevation" or "chronic relaxation" substituted, especially because it has been frequently confused in the literature with diaphragmatic hernia. In the latter condition there is a herniation of the abdominal contents through an opening in a normally situated diaphragm.

The rarity of eventration especially as compared with hernia of the diaphragm should be emphasized. In 1916 Bayne-Jones[1] collected 41 cases; Korns,[2] in 1921, considered 22 cases as proved and 43 as probable. Up to 1926, about 100 cases of eventration had been reported in the literature, many of which are doubtful because of lack of autopsies, whereas up to 1930, 1,435 cases of diaphragmatic hernia (congenital, acquired, and traumatic) had been reported. Bayne-Jones states that diaphragmatic hernia occurs thirty-seven times as frequently as eventration.

In the great majority of reported cases the eventration has occurred on the left side. Its right-sided appearance in the case forming the basis of this paper must be considered most unusual, since only ten cases have been reported to date, the last as recently as July, 1935.[3]

M. N., a white male, was admitted to the Bliss ward of the Roosevelt Hospital, service of Dr. Philip Van Ingen, Feb. 10, 1934, at four weeks of age. From the time of his birth at the Woman's Hospital it was noted that the baby was cyanotic and moderately dyspneic. A tentative diagnosis of an enlarged thymus was made, and x-ray taken the day after birth revealed what was thought to be a diaphragmatic hernia, with the liver in the right chest. During his stay of twenty-nine days at the Woman's Hospital, the infant was fed by gavage, being unable to take the nipple properly. For the first fourteen days of life he received breast milk, and subsequently an evaporated milk formula.

The *family history* was negative; two siblings, three years and fourteen years old, are alive, well, and apparently without abnormalities.

Examination on admission revealed a cyanotic, undernourished white child of twenty-nine days, breathing rapidly and appearing chronically ill. The positive physical findings were as follows: *Chest:* There was dullness and diminished breathing at the right base posteriorly below the angle of the right scapula. *Heart:* Not apparently enlarged, rate rapid, and over the entire precordium there was a loud systolic murmur, heard maximally at the apex. An x-ray taken on February 14 was reported by Dr. W. H. Boone as follows:

Chest: Several films of the chest demonstrate a dense shadow of the right side which extends to the third rib anteriorly. There are gas shadows outlining the colon lateral to and slightly below this shadow. The heart shows some displacement to the left side. The liver shadow is not outlined in the normal position. In view of the history and x-ray examinations, we believe this to be an upward and medial rotation of the liver, probably through a congenital hernia of the diaphragm (Figs. 1, 2, 3, and 4).

A second roentgenographic and fluoroscopic examination on February 25 revealed the following:

Chest: Several films of the chest demonstrate the liver and transverse colon to extend to the third rib anteriorly on the right side. At fluoroscopic examination the left leaf of the diaphragm descended well at inspiration and there was moderate descent of the right side. Two of the films outline what appears to be a thin leaf of the diaphragm of the right side in its outer third. This is fairly well shown because of a large amount of gas in the transverse colon between the lateral chest wall and the upwardly rotated liver.

Findings: Congenital deformity of the right abdomen and chest with liver and transverse colon displaced upward into the right chest cavity and showing only a limited movement. There was no evidence to indicate an absence of the diaphragm on this side.

The laboratory findings were essentially negative.

Course.—The infant was fed on an evaporated milk formula by means of a Breck feeder. Feeding was difficult with frequent regurgitation, apparently due to gas. Hypodermoclyses were given every two or three days as needed, and the patient was kept in a semiupright position. The weight remained practically stationary during the child's stay in the hospital. On April 3 the child developed pneumonia, and death ensued on the following day, i.e., on the eightieth day after birth. The essential autopsy findings taken from Dr. Sophian's protocol are as follows:

Internal Examination.—Incision was made in midline; peritoneal cavity had a smooth surface. The ascending colon, cecum, appendix, and terminal ileum swung freely on a long mesentery and were situated to the right of the liver above the costal margin in a sac which reached as high as the third rib. The diaphragm consisted on the right side of a narrow muscular mass which at the costal attachment was 3 cm. wide. The muscular portion fused with a translucent fibrous membrane lined by serous covering which was occupied by the right lobe of the liver and the portions of intestine mentioned above (Figs. 5, 6, and 7).

Pleural Cavities: The surfaces on both sides were smooth; the right pleural cavity was about half the normal depth and the lung was about one-half the size of the left lung. From the pleural surface the diaphragm was observed to have a muscular structure only on the borders of the central tendon on the right side, and on the left side the peripheral muscular mass extended to the vertebral and costal attachment, but the central portion of the left of the diaphragm over an area 5×0.5 cm. also consists of thin translucent fibrous membrane without muscular tissue (Fig. 8). The normal openings in the diaphragm are present without dilatation.

The *pericardial* cavity was normal.

The *heart* weighed 34 gm. and externally showed normal markings. The surface was smooth. On section the chambers of the two sides were similar in form and thickness. The pulmonary artery was narrower than normal, having a width of 2 cm. and the valve had a slitlike opening formed by the space between two cusps only, an anterior one and a posterior one. Immediately beneath the valve the membranous septum had a rather sharp, wavy outline. The width of the aortic valve was 2.7 cm., and normal free cusps were present with two coronary orifices of normal situation.

Fig. 1. Fig. 2.

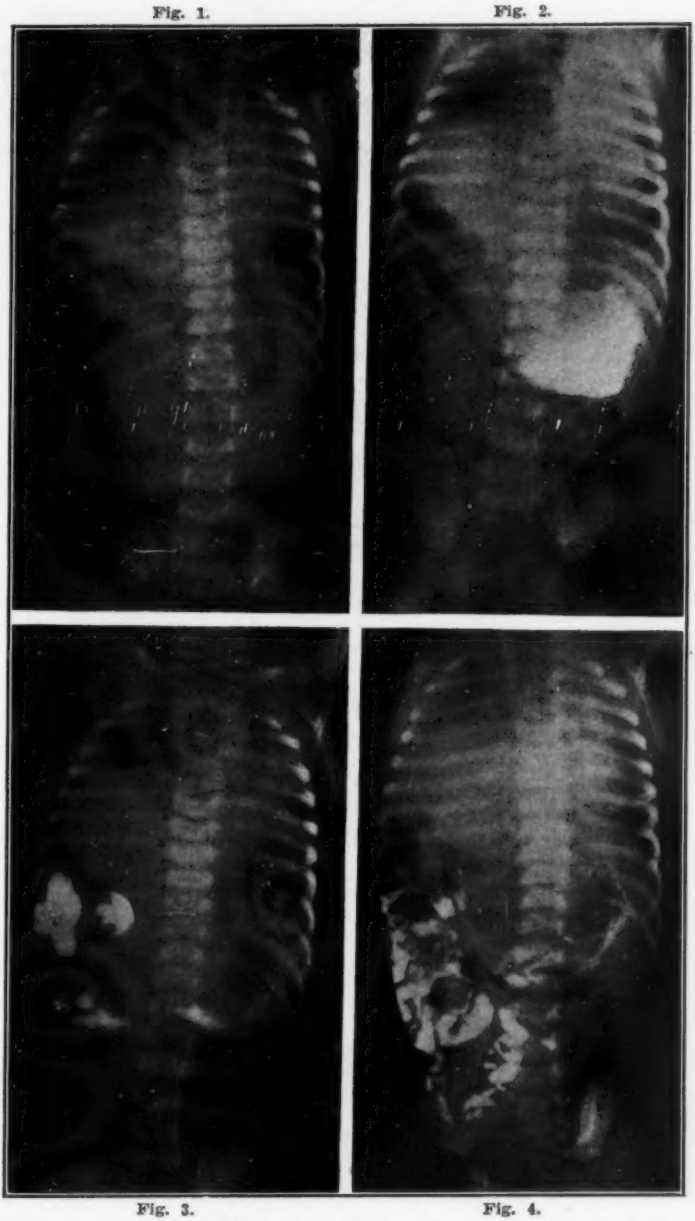

Fig. 3. Fig. 4.

Fig. 1.—Shadow extending on the right side to the third rib anteriorly; gas shadows outlining the colon lateral to and slightly below this shadow; heart displaced to the left.

Fig. 2.—Plate made immediately after barium meal, demonstrating normal position of left diaphragm.

Fig. 3.—Four-hour plate.

Fig. 4.—Eight-hour plate.

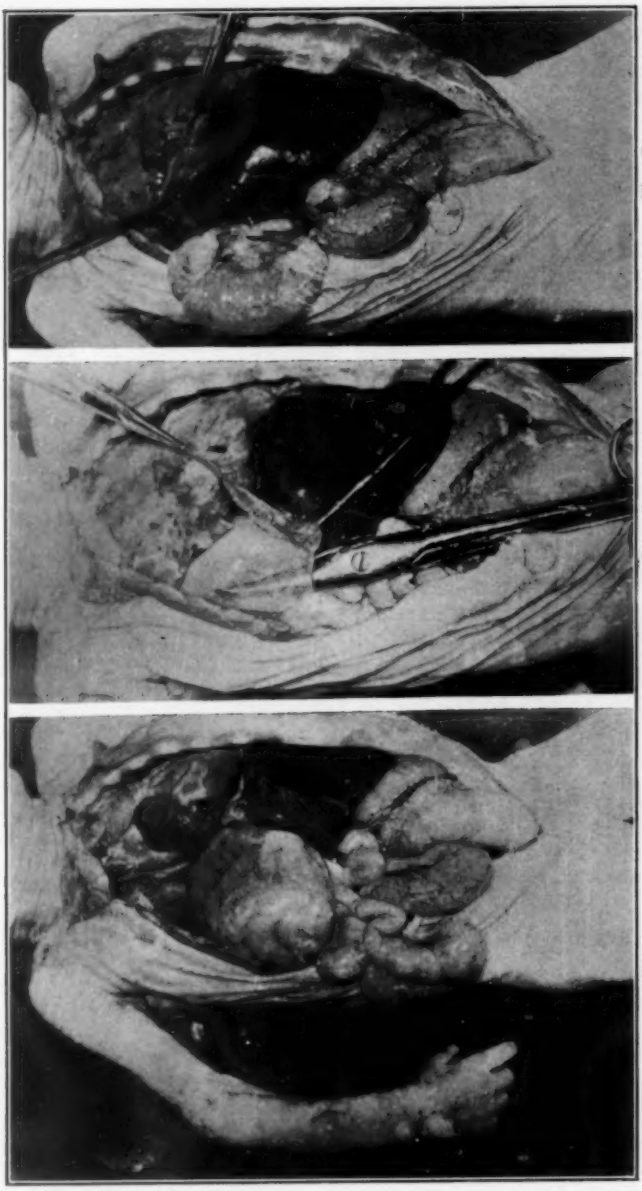

Fig. 5. Fig. 6. Fig. 7.

Fig. 5.—Showing sac in which are contained ascending colon, cecum, appendix, terminal ileum, and right lobe of liver.
Fig. 6.—Scissors inserted under sac to show translucency of membrane.
Fig. 7.—Sac opened up revealing right lobe of liver and displaced ascending colon, appendix, and terminal ileum.

Lungs: The right lung cut with increased resistance and on section the tissue was moist, with cloudy froth exuding. There was no middle lobe, and the single interlobar fissure was deficient in the midportion.

The *liver* had an abnormal form and weighed 120 gm. The right lobe was tilted so that the right surface had become the superior one and the gallbladder was posterior. There was a narrow isthmus, and the left lobe was relatively large. The falciform ligament was to the left side. The gallbladder and ducts were normal and contained brown, fluid bile.

Anatomical Diagnosis.—Congenital deficiency of the musculature of the diaphragm with eventration of the right leaf.

Displacement of the liver, with constriction of the midportion.

Congenital heart disease with interventricular septal defect and bicuspid pulmonary valve.

Compression atelectasis of right lung.

Diffuse bronchopneumonia of left lower lobe.

ETIOLOGY

It is agreed by most authors that eventration has, in the majority of cases, a congenital origin. Substantiating this belief is, first, the much more frequent occurrence of eventration on the left side, which is ex-

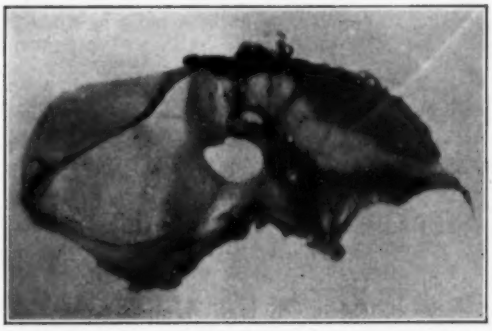

Fig. 8.—Showing almost complete absence of muscle tissue in right leaf of diaphragm and partial defect in left leaf.

plained on the basis of a more complex vascular development of the left leaf of the diaphragm, second, the finding of this anomaly in the fetus and the newborn, and third, the frequent coincidence of other congenital anomalies with eventration.

Embryologically, the primitive diaphragm develops very early, the first anlages appearing bilaterally at the level of the fourth cervical myotome whence it soon descends to the place occupied in extrauterine life, to fuse with the dorsal mesentery of the fore-gut and laterally with the pleuroperitoneal folds. The membrane thus formed separates for the first time the thoracic from the peritoneal cavity. According to Hedblum,[4] "the primitive diaphragm . . . is without any muscular constituent. Its striated muscle originates in a pair of premuscle masses lying opposite the cervical myotome in 9 mm. embryos . . . the muscle masses migrate caudally with septum and develop first in the periphery of the diaphragm. Its further centripetal extension is by pressure from

the expanding lungs, which peel off the muscle along the body wall as they advance downward. The distribution of the muscle when complete is uniform throughout."

It seems obvious, therefore, that if at an early period of embryonic life there is arrest of development of these premuscle masses, there will be a thinning of the central portion of each side of the diaphragm, producing the condition termed eventration, in which only a tenuous membrane remains in the mesial portion of the diaphragmatic leaf (Fig. 8).

It should be noted here that conditions producing increased intra-abdominal pressure, such as the growth of the abdominal organs or ascites or disturbances of the alimentary tract, such as meteorism or aerophagy, when brought to bear on an abnormally weak diaphragm may accentuate the eventration.

DIAGNOSIS

The clinical diagnosis of eventration is very difficult. The three most common symptoms are cyanosis, dyspnea, and dysphagia. The physical signs are inconstant. Tympany or dullness may be present, or gurgling sounds may be heard over the affected side.

The diagnosis is commonly made, if made at all during life, by roentgenographic and fluoroscopic examination. The x-ray picture shows a displacement of some of the abdominal contents high into the chest; as has been stated, they may reach the level of the second rib anteriorly. Fluoroscopic examination may or may not reveal the so-called "paradoxical" movement which consists in an ascent of the diaphragm on inspiration on the affected side at the same time that descent occurs on the normal or healthy side.

The condition from which eventration must be differentiated principally is diaphragmatic hernia. This difficulty is of more than academic interest inasmuch as some cases of diaphragmatic hernia may be amenable to surgical intervention, whereas in eventration the situation is usually considered surgically hopeless. Hernias may occur either through a failure of fusion of the anlages previously mentioned or through the occurrence of abnormally large normal openings, as for example, so-called esophageal hiatus hernia. (All reference to the somewhat obscure and controversial question of the terms "false" and "true" hernia are purposely omitted.) In hernia the diaphragm is normally situated and contains its normal muscular constituents.

A helpful sign in the differentiation is the usual asymmetrical movement of the costal margin. According to Hoover,[5] the diaphragm acts as an antagonist of the intercostal muscles. In the absence of weakening of the diaphragm there is a widening of the intercostal spaces on inspiration as compared with the unaffected side. This does not occur in hernia because the diaphragmatic musculature is normal. A most important point in the differentiation of these two conditions is the

fact that the roentgenographic picture remains constant at different examinations in eventration, whereas in hernia the picture may vary from time to time, due to a temporary reduction of the hernial sac.

Other conditions which must be differentiated from eventration are diverticulum of the cardiac end of the stomach and diverticulum of the lower end of the esophagus, in both of which conditions the diaphragm is seen intact above the barium-filled outlines. Also to be differentiated is thoracic stomach, in which, due to an incomplete descent of the stomach in embryonic life, this organ remains partially or wholly above an intact diaphragm. Congenital heart disease, asphyxia neonatorum, intracranial hemorrhage, enlarged thymus, and even pleural effusion may be suspected. If the eventration occurs on the left, displacement of the cardiac shadow to the right may cause a faulty diagnosis of dextrocardia.

PROGNOSIS

The prognosis in early infancy is usually poor, but, provided that the infant survives the first few months of life, the condition is not incompatible with normal life. LeWald[6] states that extensive defects of the diaphragm may occur without any serious disturbance to the individual, and points out that animals, including vertebrates up to mammals, have no diaphragm.

TREATMENT

Most cases require no treatment. Surgical intervention is usually contraindicated, although in one case, that of Lereh (quoted by Lord[7]), three pleats were taken in the diaphragm with subsequent good results.

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THROMBOSIS OF INTERNAL CEREBRAL VEINS IN INFANCY AND CHILDHOOD

Review of Literature and Report of Five Cases

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THROMBOSIS of the intracranial venous channels in infancy and childhood presents a bewildering variety of clinical and pathologic manifestations. When considering thrombosis of these channels, one usually thinks of an affection of the dural sinuses. The possibility of occlusion of the cerebral veins, especially of the internal group, has not been emphasized. We have been able to find reports of only twenty-one cases of thrombosis of the internal cerebral veins in a review of the literature, although it is likely that others have escaped our notice. Since the condition is so unusual and since no review of the literature has been made, it was thought worth while to study the collected cases and to record our observations in five additional cases which have come to our personal attention.

Thrombosis of the intracranial venous channels is usually classified as *primary* (marantic, autochthonous) or *secondary* (infectious, septic). As a result of an earlier study,[1] it has seemed to us that a third or *combined type* should also be considered in which thrombosis is apparently due to the accumulated effects of both a focal infection and a general disease. The primary or autochthonous type, occurring either in infancy or later life, follows states of debility or dehydration, gastrointestinal disturbances, and anemia. The larger channels, notably the superior longitudinal sinus, are commonly affected. In infancy and childhood, the septic type occurs most commonly after infection in the middle ear and mastoid. The combined type occurs in malnourished or dehydrated children who have developed otitis media. We believe that the otitis is responsible for the early development of a thrombus in the genu of the lateral sinus. The quantitative and qualitative changes in the blood favor a widespread involvement of the venous channels by retrograde extension from the original focus.

Thrombosis of the cerebral veins is found less frequently. It ordinarily occurs as a result of retrograde extension into these vessels of a thrombus originating in one of the dural sinuses. Thrombosis beginning in the external cerebral veins is most commonly secondary to suppurative processes in the subdural and subarachnoid spaces. Isolated cases of primary thrombosis of these veins have been described. Thrombosis of the internal cerebral veins, however, is usually of the

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primary or combined type. The thrombus may first develop within the system of internal cerebral veins or may result from a retrograde extension from the dural sinuses.

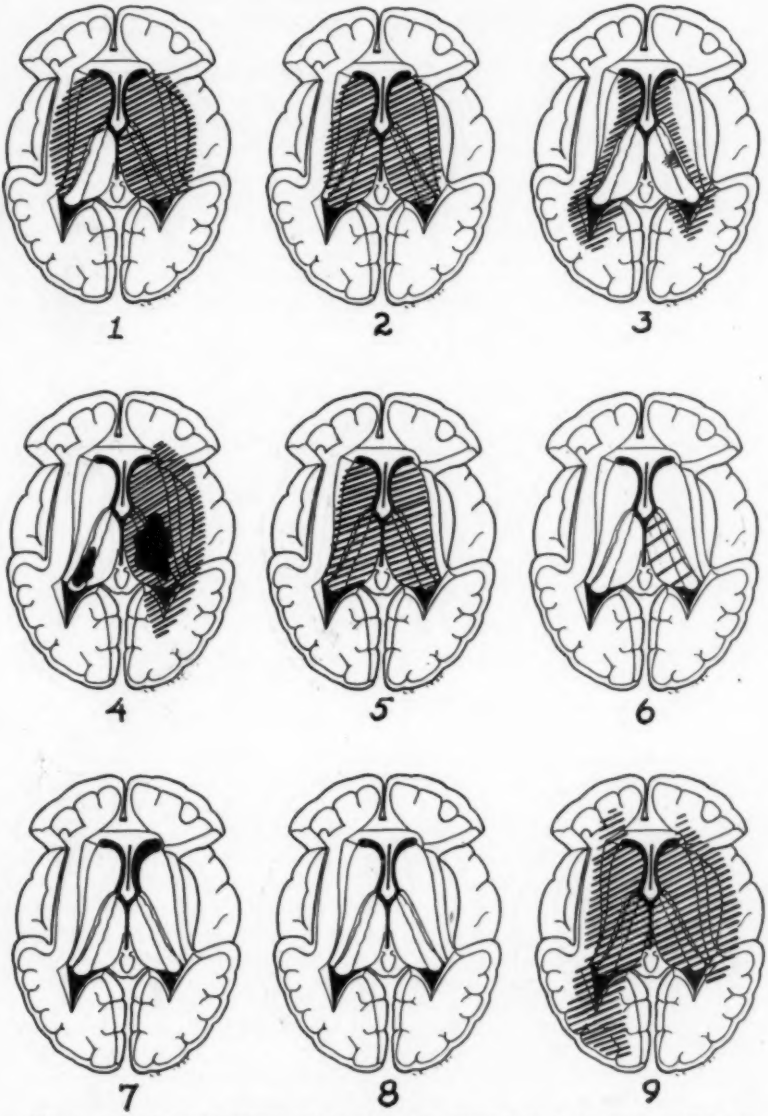

Fig. 1.—Location and extent of the lesions in Cases 1 to 9 as listed in Table I. Oblique lines represent involvement of cerebral tissues, the proximity of the lines indicating degree of softening. Small patches of oblique lines indicate scattered petechial hemorrhages. Solid black areas indicate blood clots. These diagrams were taken in most instances from the description of the author, for illustrations were found only in a few cases.

REVIEW OF THE LITERATURE

The first cases of thrombosis of the internal cerebral veins to be reported occurred in adults. The first case that we have been able to discover was that of Morgagni.[2]

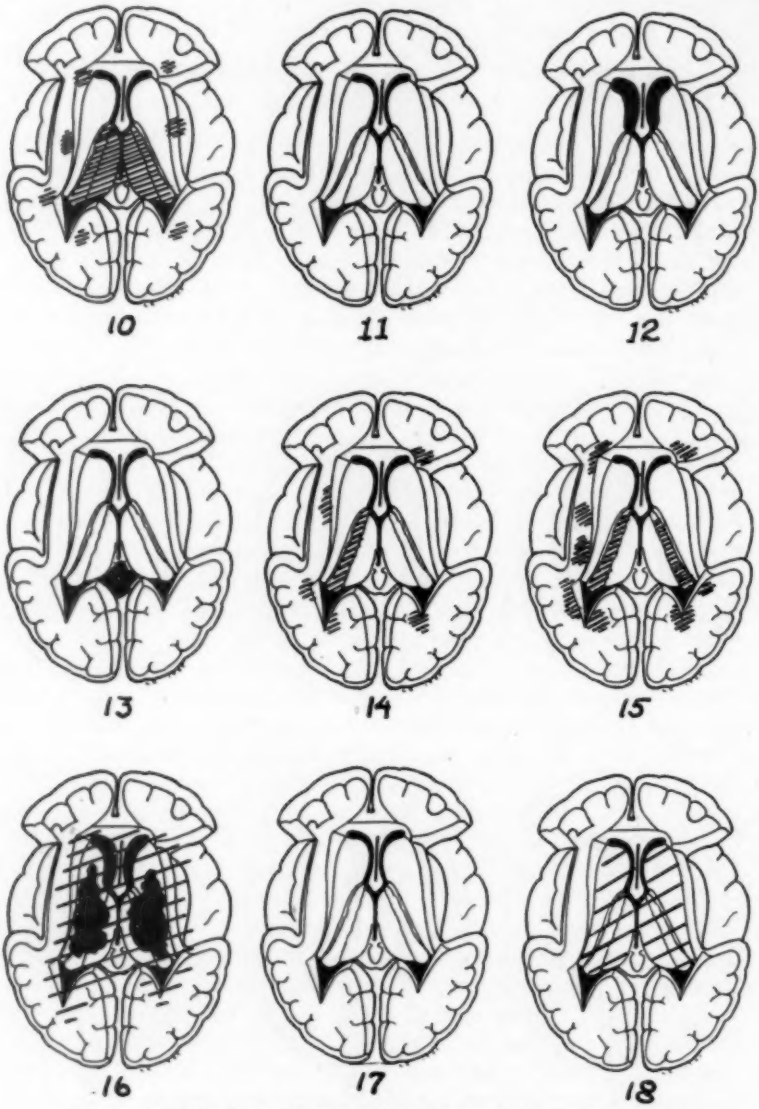

Fig. 2.—Location and extent of lesion in Cases 10 to 18 of Table I.

The lesion developed after childbirth. His description of one of the effects of obstruction of the internal cerebral veins is so characteristic as to warrant its quotation:

> In the dissection of Madame de Mauvoisin who died in childbed, apoplectic and epileptic at the same time, I observed that the whole left ventricle of the brain was full of watery blood, serous, putrid and discolored, and that the veins of the plexus restiformis together with the arteries were tumid, as if inflated and of a black color.

In 1865 Andrews[3] described the pathologic changes resulting from obstruction of the veins of Galen. A twenty-year-old woman died of cerebral symptoms developing in the course of an anemia. At autopsy there was found an extensive hemorrhagic softening of both optic thalami and the left corpus striatum.

In 1873 Parrot[4] described a case of thrombosis of the internal cerebral veins in a twenty-day-old infant, the first that we have found occurring in the earlier years of life. At autopsy the veins of Galen were incompletely thrombosed, and there was softening of the corpora striata and optic thalami. Two years later he described a second case. In 1904 Halff[5] reviewed ninety cases of marantic thrombosis of the dural sinuses, in twenty of which he found thrombosis of the veins of Galen. Four

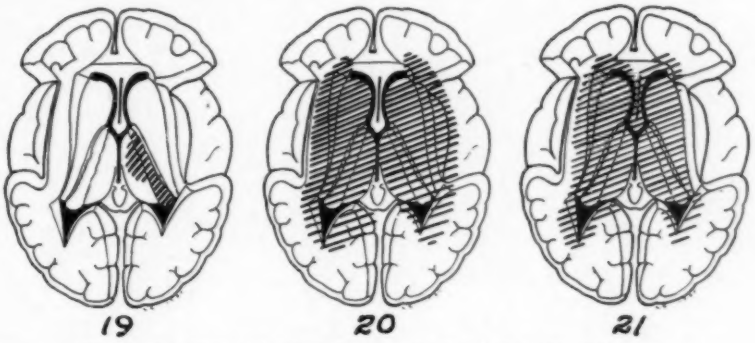

Fig. 3.—Location and extent of lesion in Cases 19 to 21 of Table I.

of these cases were in children. In 1903 Walko[6] reviewed the literature on the subject and discovered ten cases of thrombosis of the internal cerebral veins, finding only one report of this condition in a child, that of Goodall.[7] The cases of Parrot,[4] Hutinel[8] Rotch,[9] Spurrell,[10] Vaitl,[11] Delille,[12] and Fisher[13] were evidently overlooked. Since then ten additional cases have been reported, one by Hamill,[14] one by Spiller and Camp,[15] two by Halff,[5] one by Dessauer,[16] one by Wyllie,[17] three by Simpson,[18] one by Byers and Hass,[19] twenty-one cases in all.

Of the recent reports, those of Simpson, and Byers and Hass are of special interest. Simpson found records of 40 cases of thrombosis of the intracranial venous channels in infancy and childhood which had been admitted to the Hospital for Sick Children in Toronto during a period of ten years. In four of these cases thrombosis was found in the system of Galen. Two of these cases were noted in sufficient detail to be included in our table of reported cases. Byers and Hass studied a series of fifty cases of thrombosis of the intracranial venous channels in infancy and childhood. Thrombosis of the venous system of Galen was noted in seven instances, three of the primary type, two following meningitis, and two after sepsis. The detail of only one case was furnished. In Table I the essentials of the reported cases and of our own are summarized. The location and character of the gross lesions in the reported cases are shown in Figs. 1 to 3.

TABLE I

COLLECTED CASES OF THROMBOSIS OF THE INTERNAL CEREBRAL VEINS

NO.	NAME	AGE SEX	ETIOLOGIC FACTOR	CLINICAL PICTURE	PATHOLOGIC FINDINGS
1	Parrot 1873	20 days M	Unknown.	Petechial hemorrhages in skin. Nystagmus. Jerking of head to right. Pulse 120. Temperature 40° C.	Thrombosis of all sinuses except superior longitudinal and torcular Herophili. Veins of choroid plexus filled with clot. Incomplete thrombosis of the veins of Galen. Softening of both corpora striata and right optic thalamus and walls of lateral ventricles.
2	Parrot 1875	8 days F	Unknown. Infection (?)	Symmetrical ulceration in posterior part of palatine vault. Death in 6 days. Temperature 40.3° C.	Thrombosis of veins of Galen, of choroid plexuses, and vein of the right corpus striatum. Thrombus of torcular Herophili which extended into neighboring sinuses. Clot in right lateral ventricle. Softening of walls of lateral ventricles.
3	Hutinel 1877	2½ mo. F	Unknown.	Convulsions.	Thrombosis of radicals of vena terminalis. Softening of walls of lateral ventricles.
4	Hutinel 1877	2 yr. 9 mo. F	Unknown. Diarrhea. Infection (?)	Perineal ulcerations and gangrene. Pemphigus. Diarrhea.	Thrombosis of superior cerebral veins; and veins of Galen and their tributaries. Petechial hemorrhages in right thalamus and corpus striatum. Hemorrhagic spots with softening in white substance of both hemispheres. Congestion of lungs. Enlarged tracheal lymph nodes.
5	Rotch 1883	6 wk. M	Weight loss. Vomiting. Diarrhea for 13 days.	Onset with rhythmic contractions of extremities. Opisthotonos. Deviation of head and eyes. Death 24 hours after onset of nervous symptoms.	Thrombosis of straight sinus, and adjoining part of superior longitudinal sinus, veins of choroid plexus and continued into straight sinus. Floors of lateral ventricles covered with thrombosed vessels.
6	Spurrell 1896	13 or 14 yr. F	Anemia.	Onset with headache. Neck rigidity and retraction. Pupils fixed to light. Slight optic neuritis. Temperature 104-105° F. Death in 8 or 9 days.	Right vein of Galen and great vein of Galen occluded by clot which projected 0.1 in. into straight sinus. Right optic thalamus enlarged.

TABLE I—CONT'D

NO.	NAME	AGE SEX	ETIOLOGIC FACTOR	CLINICAL PICTURE	PATHOLOGIC FINDINGS
7	Vaitl 1898	1 yr. M	Bronchopneumonia following laryngeal diphtheria.	Details not known.	Thrombosis of vein of Galen, straight sinus, superior (posterior part) and inferior longitudinal sinuses, both transverse sinuses, and petrosal sinuses. Slight dilatation of right lateral ventricle. Diphtheria of larynx and trachea. Bronchopneumonia. Nephritis.
8	Goodall 1899	8 yr. F	Scarlet fever 11 days.	Onset with generalized convulsions. Rigidity. Coma. Pupils contracted. No optic neuritis. Fever 12 days, 41.8° C. before death. Death in 2 days.	Thrombosis of straight sinus, veins of Galen, and choroid plexus.
9	Delille 1900	14 mo. F	Cachexia. Gastrointestinal disturbance. Bronchopneumonia.	Child was motionless. Members flaccid. Pupils dilated. Coma.	Thrombosis of right lateral sinus, superior longitudinal sinus and its affluents and veins of Galen and their tributaries. Softening of central gray nuclei. Softening and hemorrhage in periventricular white substance. Especially caudate nucleus, and optic thalami. Bronchopneumonia. Lung abscess.
10	Fisher 1901	5 mo. F	Diarrhea, vomiting 4 days.	Onset with spasmodic opisthotonus Rigidity of all limbs, persistent on left side. Nystagmus. Squint. Exaggerated knee jerks. Temperature 103-104° F., rise to 106° on day of death, 7 days after onset.	Thrombosis of both choroidal veins and veins of Galen to beginning of straight sinus. Softening of optic thalami and corpus callosum. Punctiform hemorrhages in walls of lateral ventricles. Choroid plexuses enlarged and distended with thrombus. Bronchopneumonia. Mucopus in both tympanic cavities.

TABLE I—CONT'D

NO.	NAME	AGE SEX	ETIOLOGIC FACTOR	CLINICAL PICTURE	PATHOLOGIC FINDINGS
11	Fisher 1901	11 mo. M	Bronchopneumonia 7 days.	Onset with drowsiness lasting 3 weeks. Head retracted 3 weeks before death. Temperature elevated almost to 105° F. for 3 weeks.	Thrombosis of small veins of Galen, some of superficial cerebral veins, and left lateral (partially), and left cavernous sinuses. Brain grossly normal. Pus in tympanic cavities. Consolidation of upper lobe of right lung.
12	Hamill 1903	15 days M	Unknown.	Elevated temperature from second day. Rash on seventh day. Rapid respiration. On fourteenth day twitching of right eye. On sixteenth day temperature rose to 106.8° F.; vomiting altered blood. Passed several tarry stools. Facial cyanosis.	Thrombosis of superior longitudinal sinus, left lateral sinus, straight sinus, and vena Galeni magna, and of some of superior cerebral veins. Hemorrhage over brain anteriorly on superior surface. Both ventricles dilated and contained blood. Umphilitis. Thrombosed umbilical arteries. Anomalous kidneys.
13	Spiller and Camp 1904	7 yr. M	Unknown.	Onset with headache and vomiting. Unconscious 2½ hr. later. Veins of face engorged. Pupils dilated and immobile. Temperature 99.4-100° F. Death in 23 hr.	Clot occluding jugular foramen. Thrombosed united veins of Galen. Superior longitudinal sinus calcified in middle part. Hemorrhage into lateral ventricle.
14	Halff 1904	1 yr. 4 mo. M	Diphtheria?	Symmetrical gangrene of fingers (following diphtheria). Convulsions 1 hour before death.	Thrombosis of superior longitudinal sinus, sinus rectus, vena Galeni magna and its branches. Petechial hemorrhages in both sides of the brain. Edema of brain. Ulceration of gums, hypertrophied tonsils and cervical lymph adenitis. Gangrene of distal phalanges of fingers.

TABLE I—CONT'D

NO.	NAME	AGE SEX	ETIOLOGIC FACTOR	CLINICAL PICTURE	PATHOLOGIC FINDINGS
15	Halff 1904	2 yr. 3 mo. F	Pneumonia following diphtheria and measles.	Details not known.	Thrombosis of vena Galeni magna. Numerous petechial hemorrhages in white matter of both hemispheres. Gray matter grayish red. Diphtheritic laryngitis and tracheitis. Bronchopneumonia. Embolism of both pulmonary arteries. Miliary tuberculosis of spleen. Tracheal and bronchial lymph node tuberculosis.
16	Dessauer	2¼ yr. F	Pulmonary disease. Vomiting. Diarrhea. Measles.	Pale. Rachitic. Poorly nourished. Scalp veins engorged. Twitching of feet and hands and the muscles of eye. Unconsciousness followed by death on same day.	Thrombi in basal sinuses. Thrombosis of great vein of Galen. Lateral ventricles enlarged and filled with clotted blood. Hemorrhagic infarcts of both hemispheres. Bronchiectasis.
17	Wyllie 1924	16 mo. M	Pneumonia 6 days.	Onset with drowsiness and quietness. Twitching of limbs on ninth day. Unconscious. Bulging fontanel. Neck rigid. Death in 1 day.	Thrombosis of superior longitudinal sinus and its affluents, left lateral sinus, and veins of Galen, and all other sinuses. No hemorrhages or softening in brain tissue. Consolidated right lung. Pus in right mastoid cells.
18	Simpson 1932	Newborn	Unknown.	Cephalhematoma and convulsions.	Veins of Galen and of choroid plexus thrombosed. Laceration of caudate nucleus and optic thalamus. Hemorrhage into ventricle.
19	Simpson 1932	7½ mo. F	Unknown. Recurrent colds and G. I. upsets.	Irritable and drowsy. Eyelids and right side of face puffy. Rigidity of neck. Increased deep reflexes. Bulging fontanel. Well 15 days. Then found dead.	Thrombosis of superior longitudinal sinus and its affluents. Area of hemorrhage in right lateral ventricle was degenerated and contained a thrombosed vessel which was partly recanalized.

TABLE I—CONT'D

NO.	NAME	AGE SEX	ETIOLOGIC FACTOR	CLINICAL PICTURE	PATHOLOGIC FINDINGS
20	Simpson 1932	1 yr. M	Unknown.	Onset with drowsiness for 2 days. Rolling eyes. Convulsions on right side. Strabismus. Full fontanel. Temperature 106° F. before death. Xanthochromic spinal fluid. Died 1 day after onset of nervous manifestations.	Thrombosis of superior and inferior longitudinal sinuses, and part of lateral sinuses, the veins of Galen, and of choroid plexuses, and cerebral and cerebellar veins. Petechial hemorrhages in both hemispheres, especially the basal ganglia.
21	Byers and Hass 1933	1 Yr. F	Vomiting. Diarrhea 17 days.	Convulsions on fourth day. Next day rhythmic convulsive movements. Rigidity. Generalized convulsions. Edema of eyelids. Bulging fontanel. Edema of optic disc. Xanthochromic spinal fluid. Death 2 days after onset of nervous symptoms.	Thrombosis of superior longitudinal sinus and its affluents, middle part of each lateral sinus, straight sinus, veins of Galen, left superior petrosal sinus, right cavernous sinus, and inferior longitudinal sinus. Cortical and meningeal hemorrhages with extensive necrosis in wall of lateral ventricles.
22	Authors	2 yr. F	Marasmus. Debility. Endocarditis.	Twitching of right hand 1 week before exit. Generalized convulsions a few hours before death. Coma. Trismus. Neck rigidity. Xanthochromic spinal fluid. Death 1 wk. after onset of nervous symptoms.	Thrombosis of superior longitudinal sinus and its affluents, superior cerebellar veins, inferior sagittal sinus, large and small veins of Galen. Basal ganglia grossly normal. Zone of softening in left hemisphere above the corpus callosum which extended into dilated left ventricle. Vegetations on tricuspid and mitral valves. Thrombi in pulmonary artery.
23	Authors	20 days F	Prematurity. Diarrhea. Dehydration 11 days.	Loss of weight since fourteenth day. Liquid stools. Extensor spasms. dration. Positive blood Wassermann reaction. Death at 20 days.	Thrombosis of left terminal vein. Hemorrhagic softening of left corpus striatum and internal capsule. Right middle ear and mastoid contained turbid fluid.

TABLE I—CONT'D

NO.	NAME	AGE SEX	ETIOLOGIC FACTOR	CLINICAL PICTURE	PATHOLOGIC FINDINGS
24	Authors	1½ yr. F	Tuberculosis 9 mo.	Fever. Anorexia. No gain in weight. Diarrhea. Listlessness. Emaciation. Coma on day of death.	Thrombosis of superior longitudinal sinus to torcular extending into straight sinus and venous system of Galen. Petechial hemorrhages in walls of lateral ventricles. Softening in ventral part of corpus callosum. Four tuberculomas in cerebellum. Tuberculous meningitis. Tuberculosis of lungs and lymph nodes. Otitis media.
25	Authors	13 mo. M	Pertussis 3 mo. Bronchopneumonia 2 weeks. Left otitis media 4 days.	Onset with pneumonia and coma 2 weeks before death. Improved 5 days before death. Then again became comatose. Rapid respirations. Bilateral otitis. Trismus. Eyes deviated. Nystagmus. Neck rigid. Temperature 107° F. just antemortem.	Choroidal veins, veins of Galen, and straight sinus thrombosed. Softening of basal ganglia. Bilateral otitis media. Miliary tuberculosis of lungs. Tuberculous meningitis.
26	Authors	15 mo. F	Diarrhea and vomiting 3 weeks.	Convulsions 5 days before death. Coma. Left facial twitching. Deviation of eyes. General cyanosis. Temperature 102-108° F. Xanthochromic spinal fluid.	Thrombosis of left lateral sinus, vein of Galen and its radicals. Bilateral otitis media, more on left. Lateral ventricles dilated and filled with blood-stained fluid. Hemorrhagic softening of corpora striata, softening of optic thalami.

REPORT OF CASES

The following cases, five in number, were discovered in a review of the protocols of 12,500 autopsies which have been performed at the Los Angeles County Hospital in a period of sixteen and one-half years.

CASE 1.—(Case 22 of Table I.) Localized and generalized convulsions in a two-year-old infant. Xanthochromic spinal fluid. Death in seven days. Thrombosis of the superior longitudinal and inferior longitudinal sinuses with extension into internal cerebral veins. Hemorrhagic softening about left lateral ventricle.

A two-year-old female child was brought into the Los Angeles County Hospital in coma. A week before her admittance a twitching in the right hand was observed by her parents. Two days prior to her entrance she became comatose. The child had been born prematurely and had always been delicate.

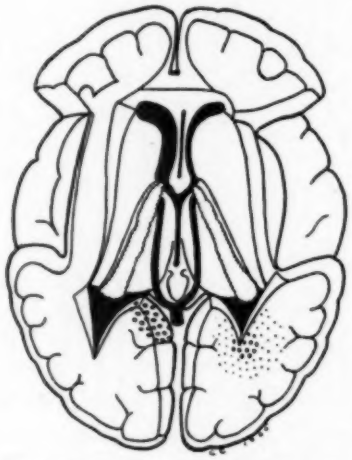

Fig. 4.—Authors' Case 1 (Case 22 of Table I). Location and extent of lesion represented diagramatically. The left lateral ventricle is enlarged. The portion of the internal venous system involved by the thrombus is indicated in solid black (small veins of Galen). Large dots indicate petechial hemorrhages; small dots indicate softening. Degree of involvement in Figs. 4 to 8 is indicated by the interval between dots.

Examination revealed an extremely pallid infant frothing at the mouth. Respirations were rapid and shallow; the pulse was 240 per minute. Every two or three minutes generalized convulsions occurred and could be provoked at any time by touching any part of the child's body. The pupils were widely dilated and did not react to light. The jaws were tightly clenched which made examination of the throat impossible. There was some rigidity of the neck. Spinal puncture revealed a yellowish slightly cloudy fluid under increased pressure, with 35 cells to the cubic millimeter. The child died a few hours after admittance to the hospital.

At necropsy, the superior longitudinal sinus, the superior cerebral veins, the superficial middle cerebral vein, the superior cerebellar veins, the inferior sagittal sinus, the great cerebral vein and both internal cerebral veins were found to be thrombosed. The pia-arachnoid was edematous and cloudy throughout with a small amount of fibrinous exudate along the right superior cerebral veins. On the mesial surface of the left hemisphere just above the corpus callosum there was an oval-shaped, necrotic

hemorrhagic area. This area extended into the dilated left lateral ventricle and was surrounded by a zone of softening which contained many petechial hemorrhages. Another area of similar description was found in the anterior part of the right occipital lobe. The veins draining this area were thrombosed (Fig. 4). The basal ganglia showed no gross changes. Small translucent vegetations were found on the tricuspid and mitral valves. All arteries of the right lung were filled with thrombi. The middle ears contained a small amount of mucoid pus. Sections from the margins of the necrotic areas disclosed numerous circumscribed hemorrhages. Microscopically the capillaries were found to be distended with blood. The areas of softening contained a central zone of necrosis surrounded by a zone of petechial hemorrhages. Cultures from the superior longitudinal sinus, from the infarcted areas in the brain, and from the heart valves showed a hemolytic streptococcus.

Comment.—This case of thrombosis of the internal cerebral veins has two evident etiologic factors, debility and infection. The child had been born prematurely and had always been rather delicate so

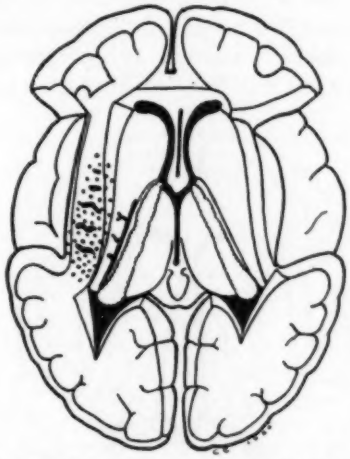

Fig. 5.—Authors' Case 2 (Case 23 of Table I). Hemorrhagic softening of left centrum secondary to thrombosis of left terminal vein and its radicals.

that the formation of a thrombus was probably favored by a slow blood current as well as by qualitative changes in the blood. The toxins from the organism may have damaged the endothelial lining of the sinuses so that the deposition of the clotting elements was favored. A similar process was found in the right pulmonary artery. Thrombosis of the venous system of Galen was evidently secondary to that in the dural sinuses as indicated by the absence of marked changes in the basal ganglia.

CASE 2.—(Case 23 of Table I.) Extensor spasms in twenty-day-old premature infant. Congenital syphilis. Death in two days. Thrombosis of the left terminal vein. Hemorrhagic softening of the left corpus striatum.

A premature female infant weighing 4 pounds and 15 ounces was born on March 17, 1930, by cesarean section. The mother had a tuberculous involvement of the hip and lungs and a positive blood Wassermann reaction. Weight loss began on March 25

and persisted until the infant weighed 14 ounces less than birth weight. Seven days later there were several green liquid stools. Four days later extensor spasms were noted. Pustules of staphylococcic origin were observed on the scalp. Dehydration became marked. The temperature ranged between 97 and 101° F. In the twenty-four hours prior to death 99° F. was the highest recorded temperature. Four stool examinations were negative. The patient died two days after onset of cerebral symptoms.

At necropsy the leptomeninges, particularly those over the cerebellum, were moderately congested. On separating the hemispheres from above there came into view a large area of hemorrhagic softening. The softened area was the left corpus striatum and internal capsule. The left terminal vein contained a recent thrombus which on microscopic examination proved to be antemortem. Petechial hemorrhages were found in the surrounding brain substance (Fig. 5).

The right middle ear and mastoid antrum contained a moderate amount of thin turbid fluid. Smears from the mastoid antrum showed gram-positive diplococci.

Comment.—A number of factors—congenital syphilis, loss of weight and diarrhea—occurring in a premature infant produced a state which was favorable to thrombus formation. It is not likely that the pustules on the scalp bore any etiologic relationship to the thrombosis since no

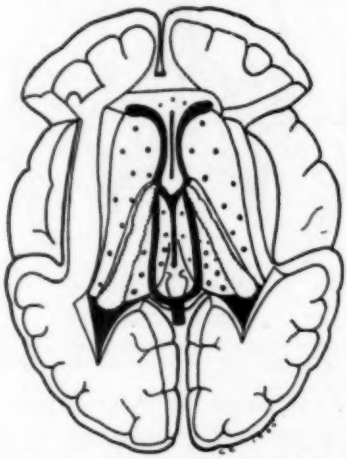

Fig. 6.—Authors' Case 3 (Case 24 of Table I). Thrombosis of small veins of Galen and petechial hemorrhages in walls of ventricles without gross softening. Softening of the ventral surface of the corpus callosum was present but could not be shown in this drawing.

evidence of direct extension or inflammation was found. It is of interest to note in this case that thrombosis began in the left terminal vein with characteristic resultant changes in the left basal ganglia.

CASE 3.—(Case 24 of Table I.) Cachexia following pulmonary tuberculosis in a one and one-half-year-old infant. No cerebral or meningeal manifestations. Coma and death. Multiple tuberculomas of the brain and tuberculous meningitis. Thrombosis of the superior longitudinal and straight sinus with extension into the venous system of Galen. Hemorrhagic softening about lateral ventricles.

A Mexican girl one and one-half years old was known to have had tuberculosis since the age of nine months. There was a history of fever, refusal to eat, no gain in weight, diarrhea, and listlessness.

The child was emaciated. Râles and altered breath sounds were heard over both lungs. The eardrums were dull. Roentgenograms showed advanced pulmonary tuberculosis. The temperature varied between 98.6 and 104.4° F. Two days before death no signs of meningeal irritation were found. She became comatose on the day of death.

At necropsy a thrombus was found in the superior longitudinal sinus as far as the torcular, extending into the straight sinus and the venous system of Galen and its radicals. Petechial hemorrhages were observed in the walls of the lateral ventricles, but extensive softening did not occur (Fig. 6). The ventral portion of the corpus callosum showed an extensive red softening. Four tuberculomas were found in the cerebellum. Miliary tubercles were also found in the exudate about the base of the brain. The middle ears were filled with purulent matter. Caseous tubercles

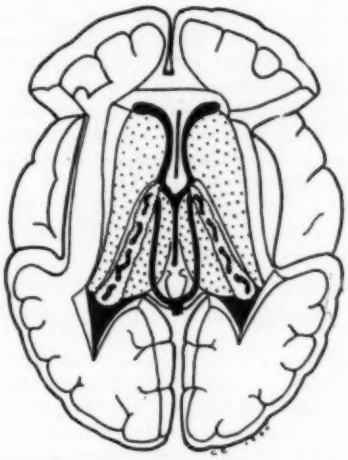

Fig. 7.—Authors' Case 4 (Case 25 of Table I). Thrombosis of small veins of Galen and choroidal veins. Softening of basal ganglia.

were found in both lungs and a number of cavities in the right upper lobe. The tracheobronchial and mesenteric lymph nodes were enlarged and caseated.

Comment.—In this case thrombosis was probably favored by cachexia incident to pulmonary tuberculosis and dehydration resulting from diarrhea. It is of interest to note that multiple tuberculomas were found in the cerebellum. In this case the bilateral otitis probably played no important part in producing the thrombosis. The absence of nervous manifestations may be explained by the absence of gross secondary changes in the brain, thrombosis evidently being a preterminal event.

Case 4.—(Case 25 of Table I.) Pneumonia followed by otitis media. Recurrent coma. Signs of meningeal irritation. Conjugate deviation of eyes. Miliary tuberculosis of lungs and meninges. Thrombosis straight sinus extending into venous system of Galen.

A white boy thirteen months old was well until three months prior to his admittance to the Los Angeles County Hospital. Two weeks before he was brought to the hospital, he developed pneumonia and became comatose. Five days before his admittance he rallied and showed improvement, but the day before, he again lapsed into coma. The left ear began to drain five days before entrance. He had not vomited nor had any convulsions.

Examination revealed an undernourished, cyanotic, and comatose male infant of one year of age. His respirations were rapid and jerky. The pulse was fast and thready. The left ear was draining. The right tympanic membrane was incised because it was reddened and bulging. The pharynx was injected. There were râles and impaired resonance over both lungs. A marked trismus was present. The eyes were deviated to the left. Nystagmus with the rapid component to the left was observed. The neck was rigid to flexion in anterior and posterior direction, but the Kernig and Brudzinski signs were negative. The temperature, which was 104° F. on admission, rose to 107° before death. A respiration rate of 64 was noted just before death, which occurred three and one-half hours after admission to the hospital.

At necropsy the leptomeninges were found to be markedly injected and a few small tubercles were found. Sections through the brain showed advanced degree of softening of the basal ganglia on each side. The choroidal veins, the veins of Galen, and the straight sinus were thrombosed (Fig. 7). There was a marked bilateral purulent otitis media. The smears from the middle ears revealed a few gram-negative organisms resembling *B. influenzae* and occasional gram-positive diplococci. The lungs showed diffuse miliary tuberculosis with a few patches of bronchopneumonia in the base of the right lung.

Comment.—In this case, tuberculosis again played an important part in the production of the thrombus. From the extent of involvement one would conclude that thrombosis began in the veins of Galen or at the juncture of the great vein and the straight sinus.

CASE 5.—(Case 26 of Table I.) Acute gastroenteritis followed by convulsions in female infant. Death after six days. Thrombosis of straight sinus and venous system of Galen. Hemorrhagic softening of basal ganglia.

A white girl fifteen months old was admitted to the Los Angeles County Hospital on Aug. 13, 1934, because of an illness which was characterized by three weeks of persistent diarrhea and vomiting. Convulsions had set in three or four days prior to entry to the hospital.

The child proved to be well nourished. In a few hours she became deeply comatose. Some left facial twitchings were observed, and the eyes were deviated to the right. The next day she had a left-sided convulsion which soon became generalized. Constant movements of the arms and legs were noted thereafter. On the following day paracentesis of the bulging eardrums yielded frank pus. That day she had several green liquid stools. General cyanosis was present during the last thirty hours. The temperature fluctuated between 102 and 108° F. but dropped to 99° prior to death. The pulse averaged 160 and was of poor quality. The respirations were 60 per minute. The child died two days after admission.

Three spinal fluid determinations were made. On August 13 it was clear and under a pressure of 350 mm. The fluid contained 118 leucocytes per cubic millimeter, 74 per cent of which were polymorphonuclears. Benedict's solution was reduced with 7 drops of fluid. Globulin was increased. Tryptophane test was positive. The fluid withdrawn on the following day showed no organisms on smear and no growth on culture. The Levinson test was reported positive. The spinal fluid obtained on August 15 was straw colored, and 80 per cent of its 54 white cells were multinucleated. A blood study showed 2,000,000 red cells and 30,000 white cells per cubic millimeter. Ag-

glutination test for bacillary dysentery was negative. Stool cultures grew no pathologic organisms. Streptococci were found in cultures of the aural pus. Because of the spasmophilic attitude calcium and phosphorus determinations were made. These showed calcium to be 10.6 mg. and phosphorus 5 mg. per 100 c.c. blood.

At autopsy the left lateral sinus was filled with a dark clot which in itself appeared to be of postmortem origin although there were beginning adhesions to the walls and some portions of this clot were broken down. This thrombus extended back into the straight sinus. The great and small veins of Galen, the choroidal veins, terminal veins, and the veins of the septum pellucidum were filled with red thrombus. The left inferior anastomotic vein was also filled and distended with thrombus. The convolutions of the brain were somewhat flattened.

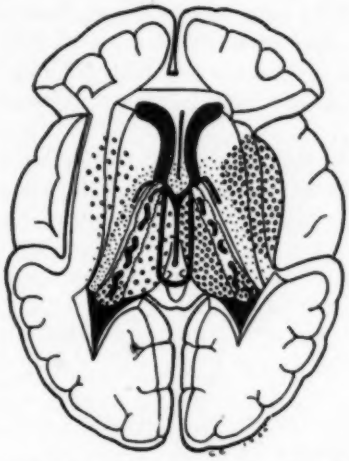

Fig. 8.—Authors' Case 5 (Case 26 of Table I). Thrombosis of small veins of Galen and choroidal veins. Softening of basal ganglia. Dilatation of the lateral ventricles.

The brain was cut in a series of coronal sections beginning at the frontal pole. The section passing through the anterior horns of the lateral ventricles disclosed these cavities to be considerably dilated and filled with a blood-tinged fluid. Another section through the corpora striata showed a softening of hemorrhagic type in these structures where the caudate and lenticular nuclei were continuous beneath the anterior limb of the internal capsule. The right basal ganglia and adjacent centrum were more extensively involved than the left. The large veins of the septum pellucidum were filled with clots and appeared as black cords running across this membrane. Further sections through the thalami disclosed a hemorrhagic softening of the medial and upper aspects of both these structures (Fig. 8). The caudate nucleus and adjacent structures were entirely free of the typical spotted hemorrhages.

Both middle ears contained yellow pus, the left more than the right. The mastoid cells were slightly moist. Most of the branches of each pulmonary artery were occluded by firm pale antemortem thrombotic material. Some hyperemic areas were observed in the mucosa of the large bowel. There was also some enlargement of the mesenteric lymph nodes.

Comment.—In this case it is natural to assume that dehydration incident to vomiting and diarrhea was the most important factor in producing the thrombosis. The otitis was most marked on the left,

and the left lateral sinus was filled with a recent thrombus. Judging by the history of early left-sided convulsions and the greater extent of the red softening on the right, one would conclude that the right-sided vessels were first affected.

ETIOLOGIC FACTORS

It seems likely that the same general and local factors are responsible for thrombosis of the internal cerebral veins as well as of the larger channels. As to *age*, it will be observed that in 8 of the 21 cases, the patient was less than six months old; and that in 19 the patient was under two years. It would seem that in infancy *sex* plays no important part. In this series of cases 15 were females, 10 were males, and in one the sex was not stated. This stands out in contrast to cases of thrombosis in adult life when the female is predominantly affected.

In infants gastrointestinal disturbance is a common cause of primary thrombosis of the internal cerebral veins.* It is not likely that anemia plays so important a rôle in the production of venous thrombosis in children as it does in adults. Syphilis was present in one of our cases but other possible etiologic factors also were present. It seems unlikely that syphilis plays any part in the production of the disease.

Tuberculosis may play a more important rôle in primary thrombosis than we have believed in the past. This disease was present in two of our five cases.

The major etiologic factors which were present in the series of collected cases are shown in Table II.

TABLE II

ETIOLOGIC FACTOR	NUMBER
Gastrointestinal disturbances	7
Pneumonia	6
Cachexia, tuberculous	3
Diphtheria	3
Measles	2
Marasmus	2
Scarlet fever	1
Anemia	1
Uncertain or unknown	9

In a number of cases more than one possible factor was present, and it was often difficult to determine just what one was actually responsible for the condition.

*The mechanism by which intracranial venous thrombosis is believed to be produced is well outlined by Gerhardt[20] and Macewen.[21] Body fluid loss because of diarrhea and vomiting causes a decrease in blood volume and an increase in blood viscosity and slowing down of the blood current in the venous channels. This state of stagnation is further aggravated by weakened cardiac action brought on by the debilitating disease. Loss of body fluids results in loss of serum from the brain as well as from the rest of the body tissues. This decrease in intracranial contents is compensated for by depression of the anterior fontanel, and if this is not sufficient to overcome the atmospheric pressure, overlapping of the cranial bones at the sutures takes place. When these fail at compensation, it is thought that the cerebral vessels and sinuses themselves become dilated. Their enlarged caliber will cause further slowing of the blood stream.

CLINICAL CONSIDERATIONS

It is to be remembered that in this condition the patient has usually been seriously ill for a variable period before the onset of the cerebral symptoms which announce the changes in the brain consequent to thrombosis. Should the development of the thrombus occur as a terminal event, cerebral changes will be minimal or grossly absent, and no nervous symptoms will be observed. In children cerebral symptoms due to the lesions occur as a rule three to twenty-one days after the onset of vomiting and diarrhea, during which time a state of disturbed nutrition and dehydration has been probably produced. In older children these manifestations are more likely to occur in the course of an acute infection or after a prolonged period of debility produced by some chronic wasting disease such as tuberculosis.

Onset.—In about twelve of the cases the onset of the condition was ushered in by a convulsion. Drowsiness was the first symptom in smaller number. In the remainder, sudden coma, opisthotonos, or headache was the first manifestation. In those instances in which the development of the thrombus was a mere incident in the closing days of life, cerebral symptoms were not observed.

Disturbance of Consciousness.—In eleven cases, some disturbance of consciousness, varying from drowsiness to coma, was present before death. To be sure, in terminal cases coma may be due to the causal disease and not necessarily to the partially developed thrombus. Neither depth of coma nor its characteristics is of any particular significance.

Febrile State.—While fever is usually present, the temperature curve is not characteristic. Furthermore, rise in temperature may be due to the original state and not to the cerebral lesion. In thirteen of the twenty-one cases, the temperature was elevated to 104° to 106° F., the highest point being reached just before death. In some cases the temperature curve showed fluctuations which descended to normal or subnormal. In two cases the temperature did not go above 100° F. Although it had been higher, in two of our cases a temperature of 99° F. was recorded just before death. The *pulse* was usually rapid and at times irregular. Respirations were variable.

Evidences of Increased Intracranial Pressure.—Manifestations of increased intracranial pressure are present in about one-half of the cases. In six cases, bulging of the anterior fontanel was observed. In Rotch's case[9] it was slightly depressed until the onset of cerebral symptoms. The facial veins were engorged in two cases. Edema of the eyelids, possibly due to vascular stasis, was mentioned as being present in two instances. The optic fundi showed evidences of pressure in two. The pressure of the spinal fluid was increased in five out of the eight cases in which a lumbar puncture had been performed.

Motor Manifestations.—Symptoms referable to the motor system were of most common occurrence. Convulsions were reported in half of the cases. These were confined to one member, were one-sided, or were generalized. In some instances the abnormal movements assumed the nature of rhythmic convulsive contractions. Trismus was present at times and a rigidity of the extremities and entire body has also been described. Although in adults it occurred quite commonly, paresis or paralysis was not observed in children. In two instances, a peculiar attitude resembling that of tetany was assumed. Nystagmus occurred three times. Oculomotor symptoms were described in eight cases. The eyes were variously described as being deviated or rolling from side to side, and in two squint was observed. An attempt to elicit deep reflexes was made in only five cases, in four of which they were increased.

The incidence of meningeal signs is somewhat uncertain. They were present in less than one-half of the cases. They were not always constant in the same patient.

Spinal Fluid.—Spinal fluid determinations were made in eight cases, in five of which it was xanthochromic. The cell count varied from normal to 1,020. Lymphocytes predominated three times, polymorphonuclears two times. Sugar reaction was reported to be normal in two and reduced in two. One of these patients had tuberculous meningitis. The globulin reaction was increased in two and normal in one. All cultures taken were sterile.

In those suffering from gastrointestinal disturbances or from acute infections, the cerebral symptoms lasted about one to seven days before death ensued.

PATHOLOGY

The pathologic picture is the result of an obstruction to the venous outflow by the thrombus. The variation in the pathologic picture depends upon a number of factors: (1) the age of the patient, (2) the length of the period of survival, (3) the point of original obstruction, (4) the rapidity and completeness of the occlusion, and (5) the presence of other lesions, such as tuberculous meningitis, which may influence the thrombotic process.

*Pathogenesis.**—The thrombus which is the ultimate cause of the red softening may develop primarily in the internal system of veins or be a secondary extension of a thrombus in the straight sinus. If originating within the system of Galen, the thrombus may either remain within these vessels to involve them in whole or in part or may spread to the straight and other sinuses. A thrombus in these vessels, therefore, may propagate itself in either direction since no valves are present

*It is not our purpose to discuss in detail the mechanism of primary or autochthonous venous thrombosis. The various theories which have been proposed are well known, and our studies have shed no further light on the problem.

to obstruct its progress. As is the rule in the larger vessels, the older parts of the thrombus are grayer in color and more solid in consistency. Partial organization may occur.

Essential Anatomy.—The intracranial venous drainage is accomplished by two systems: the external system, which through the dural sinuses and the external cortical veins drains the cortex and the greater part of the medullary substance of the brain; and the internal system or venous system of Galen, which carries the return flow of blood from the basal ganglia, the corpus callosum, the septum lucidum, gyrus cinguli, the pineal body, the quadrigeminate bodies, the crura cerebri, the region of the anterior perforated space, the upper surface of the cerebellum, and the choroid plexus.

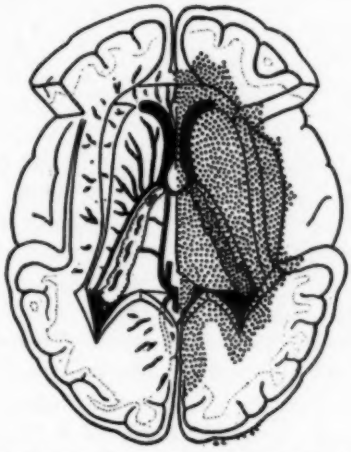

Fig. 9.—Drawing showing arrangement of internal system of veins (left) and the area drained by them (right).

The small veins of Galen are formed by the juncture of the choroidal vein, the terminal vein, and the vein of the septum pellucidum near the foramen of Monro. These veins drain the choroid plexus, the anterior portion of the corpus striatum, the septum pellucidum and the ventral part of the genu of the corpus callosum. Each small vein of Galen is divided into a straight and a curved portion. The first or straight portion of the vein runs caudally between the layers of arachnoid in the transverse cerebral fissure and receives the veins of the corpus callosum, the cerebral peduncles and the thalamus (direct lateral vein). The shorter curved or terminal portion lies beneath the curve of the splenium of the corpus callosum and receives the superior cerebellar veins, the internal occipital vein, and the posterior external vein of the corpus callosum. It joins with its fellow behind the splenium to form the great vein of Galen, a short vessel of large caliber which

empties into the straight sinus. It has no tributaries. The accompanying diagram (Fig. 9) shows the location of the vessels forming the internal venous system and the areas drained by them.

Pathology.—The pathologic picture varies considerably in the individual cases. This variation is due to the difference in the location, extent and age of the thrombus, the extent and character of the cerebral lesion, the size of the lateral ventricles, and the appearance of the contained ventricular fluid.

Location, Extent, and Character of the Thrombus: The venous system of Galen was alone involved in 6 cases, in the remaining 20 cases the dural sinuses were also affected. In 2 of these 6 cases, the radicals rather than the larger veins were involved. In 2 other instances a separate and distinct thrombus was found in the superior longitudinal sinus as well as in the system of Galen. In 4 additional cases the thrombus affected the straight sinus as well as the system of Galen. However, in 4 cases the superior longitudinal as well as the straight sinus was involved to the exclusion of both lateral sinuses. In 3 other cases one lateral sinus was also affected (left twice, right once) in addition to the straight and superior longitudinal sinus. Finally in 4 cases both lateral sinuses were involved in addition to the superior longitudinal and straight sinuses. In 9 cases in the series other channels were affected. The external cerebral veins were also thrombosed in 9 cases; in all cases but one of this smaller series the superior longitudinal sinus was also affected. In this one case, that of Fisher,[13] at least three separate thrombi were noted. This simultaneous development of thrombi in multiple situations was mentioned by Bamberg.[22]

The thrombus presents the characteristic appearance of any antemortem clot. The process may be localized or extend widely into the dural sinuses. It may begin in the system of Galen and not extend beyond it. More commonly, however, it is secondary to a thrombus, first affecting the straight sinus. It may have multiple points of origin even within the internal system of veins but this must be rare.

Changes in Cerebral Tissues: The lesions which may occur following obstruction of the internal cerebral veins are engorgement, edema, softening, and hemorrhage. In some instances, to be sure, no gross lesion was described. In such cases occlusion of the internal system was either comparatively recent or minor gross or histologic alterations had been overlooked.

The first lesion which ensues after obstruction to the venous outflow is *congestion,* although at times this may be obscured by the rapidly developing edema, hemorrhage, and softening. The affluent veins become full and tortuous, noticeable particularly in the choroid plexus and beneath the ependyma, but also manifest in the cerebral tissues themselves by their increased prominence as seen on cut section. It

is very likely that congestion actually exists in many cases in which the brain is described as normal. This finding is much more evident on microscopic sections in which the small venules stand open due to the accumulation of blood in these channels.

Transudation of fluid through the walls of the distended veins is the cause of *edema* of the surrounding tissue. As a result of his early investigations on this subject, Hutinel[8] came to the conclusion that edema was less conspicuous in cases of thrombosis of the cerebral veins in infants following dehydration. In such instances transudation was less active because of the lowered fluid content of the blood. Edema may be limited to one part such as the thalamus or may affect the entire central portion of the brain.

Softening of the affected tissue may be absent in cases of recent or incomplete obstruction on one hand or may affect large portions of the basal ganglia and the cerebral centrum on the other. In infants in particular widespread necrosis may result. This softening may or may not be of the so-called "red" variety. If hemorrhages are present, they may be spread throughout the softened area or may be limited to a bordering zone about the affected region. Simple necrosis *en masse* may take place without gross evidence of hemorrhage. This process of softening is probably the result of disturbed tissue nutrition and oxidation incident to edema and hemorrhage. In the softened areas, particularly those adjacent to the larger venous channels, notably the terminal vein, the small thrombosed vessels stand out as solid black cords.

Hemorrhage into the cerebral tissues occurred either in the form of petechial hemorrhages or as gross effusions. The size of the hemorrhage depends upon the caliber of the ruptured vessel. In most instances it is the small terminal venules which give way, and a small regional hemorrhage, frequently perivascular, results. If, however, the occlusion be abrupt, a larger vessel may rupture with gross effusion of blood, which appears as large clots, either within the softened basal ganglia or free within the ventricular cavity. Ventricular hemorrhage is not uncommon since the larger venous channels lie exposed and unsupported in the walls of these cavities. When this effusion is excessive, it may rupture through the ventricular walls to the exterior (Case 13 of Table I).

Lateral Ventricles: The choroid plexus was frequently found to be congested or edematous on one or both sides and at times was actually the seat of hemorrhage. The choroidal veins were also thrombosed at times, the thrombus in these vessels being either primary or due to retrograde extension from other vessels.

Either one or both lateral ventricles were not infrequently dilated, probably the result of increased transudation of fluid from the choroid plexuses.* The ventricular fluid may be clear and colorless. It is more commonly xanthochromic, blood tinged, or it contains gross blood clots. In eight cases the fluid was described as bloody or as containing blood clots. The blood in the fluid is evidently due to hemorrhage in the adjacent basal ganglia, corpus callosum, or the choroid plexus.

Associated Pathology.—When the central softening was extensive, the *cerebral tissue* was usually swollen and edematous and at times assumed a yellowish color. This condition was manifested externally by a flattening of the convolutions. Pial congestion has been described in some instances. In some cases the *cerebrospinal fluid* was increased in amount, probably the result of increased production by the choroid plexus. *Subarachnoid hemorrhage* is present only when the external veins are also occluded. This lesion usually follows thrombosis of the superior longitudinal sinus and its affluents, the superior cerebral veins.

Microscopic Appearance.—The histologic changes are those of edema or of hemorrhagic softening and are not characteristic of this condition. The affected tissue is disintegrated and infiltrated with red blood cells. Where the surrounding tissue is solid, the hemorrhages are more circumscribed and frequently are limited to a perivascular ring. The nervous tissue stains poorly, and ultimately all structural detail is lost. The area becomes filled with compound granular corpuscles. The small vessels show an intense congestion.

SUMMARY AND CONCLUSIONS

1. A review of the literature on the subject of primary thrombosis of intracranial venous channels disclosed sixty cases of primary thrombosis of the internal cerebral veins, twenty-one of which occurred in infancy and childhood.

2. Eight cases of primary thrombosis of the internal cerebral veins have come to the attention of the writers, in five of which the lesion occurred in infancy. These five cases form the basis of this report.

3. Gastrointestinal disturbances, pulmonary disease, and acute infections seem to be the most common predisposing factors. In a number of instances the cause is unknown. Sex is not a factor in infants. Of the twenty-one cases in children, nineteen were less than two years of age.

4. If cerebral symptoms such as coma or convulsions, together with signs of intracranial pressure, occur in an infant who has been vomiting and having diarrhea or who has been suffering from an acute infectious disease or some chronic ailment, the possibility of a thrombosis

*Ventricular distention and softening of the basal ganglia are not necessarily due to occlusion of the internal cerebral veins themselves. Obstruction of the straight sinus, especially if of long duration, may result in these changes.

of the intracranial venous channels is to be considered. If a bloody or xanthochromic fluid is recovered on lumbar puncture, this likelihood is even more definite. We know of no characteristic symptoms to suggest that the internal cerebral veins are exclusively affected. The condition, so far as we know, is uniformly fatal.

5. The pathologic picture is the result of obstruction of the venous channels by the thrombus. The variations in this picture depend upon the age of the patient, the length of the period of survival, the point of original obstruction, the rapidity and completeness of the obstruction, and the influence of other possible lesions such as tuberculous meningitis.

6. The thrombus may develop primarily in the internal system of veins or may be a secondary extension into this system from the straight sinus. The second eventuality seems to be the more common one.

7. The essential cerebral lesion is a red softening of the area drained by the occluded vessel. This softening affects predominantly the septum pellucidum, the corpus striatum, the thalamus, the ventral part of the corpus callosum, the medial aspect of the occipital lobe, or the medial superior surface of the cerebellum. The ventricular fluid is usually blood stained or xanthochromic.

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BISMUTH SUBNITRATE POISONING IN AN INFANT

Case Report

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A SEVEN-WEEK-OLD male child was admitted to the Pediatric service of Kings County Hospital with the complaints of diarrhea and cyanosis. The history was of diarrhea of one week's duration without vomiting, loss of weight, or fever. The child had been perfectly well until this time, and three weeks previously had been discharged from this institution as a healthy boarder on a diluted whole milk formula. The diarrhea began with no apparent cause, and, after it showed no tendency to clear up, a physician was called who prescribed "bismuth powder," "as much as could be placed on the tip of a teaspoon to be given with each feeding, and if the symptoms did not abate, the amount was to be gradually increased." The mother carried out these instructions implicitly and noted no diminution in the number of stools or any increase in their consistency. As directed, she increased the amount of powder until almost one teaspoonful was being given with each feeding. The child's skin took on a gradually increasing dusky color, and it was noted that he would writhe and scream soon after the ingestion of the feeding. On the third day following the onset of this cyanosis, the child was brought to us.

On admission the child presented a severe cyanosis which was as marked in the skin as in the mucosa and subungual areas. The respirations were slow and easy, the pulse rate was 120, and the temperature was 100° F. The child was apathetic and drowsy. There was a peculiar odor to the breath which did not suggest acetone or garlic. The diaper contained a loose dark stool. There were no abnormal physical signs on examination of the heart and lungs to account for the cyanosis, and the abdomen was soft with no organs palpable. The ears, nose, and throat were normal, and there were no abnormal reflexes. The pupils were of usual size and reacted well to light.

After the child was put on a skimmed milk formula, the diarrhea gradually subsided, the stools being appreciably more normal after thirty-six hours. At this time the cyanosis also began to disappear, and all symptoms were absent on the third day after admission.

The laboratory findings were negative except that the urine showed an abnormal amount of nitrites. X-ray plates of the long bones failed to reveal areas of increased density at the epiphyses. Chemical analysis of the powder used revealed pure bismuth subnitrate.

From the Pediatric Service of Dr. George E. Brockway, Jr., Kings County Hospital.

A number of deaths have been reported following the use of bismuth subnitrate. Roe[1] reports a case of infantile diarrhea in which this drug was used therapeutically. After 190 grains had been administered in forty-four hours, it was noticed that the child had become markedly dyspneic and cyanotic; he soon went into a state of shock. Despite stimulation and the use of an oxygen tent, the child expired sixty hours after the first dose had been given. The author also cites five other cases from the literature, two in which the drug was used therapeutically, and three others in which it was administered for roentgenographic purposes. All of these cases terminated fatally. This article contains an excellent bibliography.

Bohme[2] has shown that the subnitrate of bismuth is capable, under the influence of certain bacteria in the intestine, of giving off nitric acid and nitrites; the symptoms of poisoning have been shown to be due to the latter. The hemoglobin is changed to methemoglobin; thus oxygen cannot be liberated for tissue respiration, and asphyxia follows.[3]

This case is reported because of the common use of bismuth subnitrate in diarrhea and to stress the dangerous toxic effects when the drug is used with infants.

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INFECTION WITH AN ORGANISM OF THE GENUS LISTERELLA

Report of a Case of Acute Cerebrospinal Meningitis With Recovery

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HUMAN infection with organisms of the genus Listerella has been reported so infrequently that it seemed interesting to report a case of meningitis caused by a member of this group. Schultz and his associates[1] in 1934, from California, reported recovery in a case of meningoencephalitis in a woman from whose spinal fluid an organism, apparently of this group, was isolated. In the same year, Burn,[2] in New Haven, reported the finding of a morphologically similar organism in two fatal cases of purulent meningitis in newborn infants and later cared for a third fatal case in an adult, not reported. Organisms of similar nature from animal infections have been reported from a variety of locations during the past ten years. Seastone[3] has recently reviewed the literature on these varied human and animal infections. He analyzed these reports and made further observations about the known members of this group. It was found that all the strains studied were similar culturally and morphologically and all except one were related immunologically. This author suggested that all the organisms so far reported could be classified under the genus Listerella with the rabbit and gerbil strains as described in Bergey's *Manual*.

CASE REPORT

E. O., a three-year-eight-month-old Irish boy, was admitted to the Children's Hospital, Sept. 24, 1935, with a complaint of headache, fever, and delirium for one week, and a stiff neck for four days. The family history was essentially irrelevant. The patient lived with his parents in a double house in a suburb of Boston. He had no known contact with rabbits or other animals. An abscess over his left mandible had occurred, which promptly healed after incision and drainage, at one year of age. At eighteen months of age he had suffered a generalized convulsion, the cause of which was undetermined. There were no known sequelae, and there had been no recurrence of the convulsion. He developed German measles five months before entry, followed by bilateral otitis media which drained for one week and from which he seemed to recover completely.

One week before admission drowsiness was noted, and he seemed feverish. The following day he was quite talkative, occasionally delirious, and seemed to have more fever. Four days before entry he became entirely incoherent, developed a staring expression, failed to recognize familiar objects, and picked at the bedclothes. His neck was first noted to be stiff at this time. Two days before entry he vomited once after being fed. His condition remained about the same until admission to the hospital.

From the Department of Bacteriology and Immunology and the Department of Pediatrics of the Harvard Medical School, and the Infants' and Children's Hospitals.

Physical examination showed a well-developed and well-nourished boy who was alternately crying and restless and quiet and drowsy. His rectal temperature was 102.8° F., pulse rate 130, and respiratory rate 25. No petechiae or signs of a rash were seen on the skin. The pupils were equal in size and reacted normally to light. There was a slight left internal strabismus, but no nystagmus was noted. The fundi appeared normal. Macewen's sign was negative. The ear canals and ear drums appeared normal. The neck was stiff. The chest and lungs were normal. The heart was normal except for a soft, blowing systolic murmur confined to the apical region. Examination of the abdomen was negative. The deep and superficial reflexes were present and equal. The Babinski responses were normal. Kernig's sign was positive.

The laboratory findings were as follows: Urinalysis was essentially normal except for a slight trace of albumin in the admission specimen; the hemoglobin content was 77 per cent (Sahli), and there were 4,500,000 erythrocytes and 18,000 leucocytes per cubic millimeter; the differential leucocyte count was 76 per cent polymorphonuclear cells, 21 per cent lymphocytes, and 3 per cent monocytes. The blood Hinton test was negative as was the Mantoux, using 0.01 mg. of old tuberculin. The cerebrospinal fluid, obtained by lumbar puncture shortly after entry, was cloudy in appearance; the Pandy test was positive; and sugar was absent (Benedict's qualitative reagent). There were 3,600 cells per cubic millimeter, of which 68 per cent were polymorphonuclear cells and 32 per cent were mononuclear cells. A direct smear of the cerebrospinal fluid, stained by Gram's method, showed a small gram-positive bacillus. A blood culture taken the day of entry was negative.

Fifteen cubic centimeters of polyvalent antimeningococcus serum were administered intraspinally, and the same treatment was repeated the following morning. Smears of cultures of the cerebrospinal fluid grown on chocolate agar for twenty-four hours at 37° C. showed a small gram-positive bacillus, which was thought to be a member of the diphtheroid group until attention was called to the recent report by Seastone. No further serum was administered, and subsequent cerebrospinal fluid cultures verified the continued presence of the gram-positive bacillus. For the following twelve days lumbar punctures were performed daily, and from 25 to 50 c.c. of cerebrospinal fluid were removed each time.

The cell count of the cerebrospinal fluid rose to 9,900 per cubic millimeter the day following administration of the serum, but rapidly dropped and on the thirteenth day following admission was 320 per cubic millimeter. Sugar, by qualitative test, was present in the cerebrospinal fluid on the fifth day. Cerebrospinal fluid cultures were positive for the first six days after entry. The temperature varied from 102 to 105° F. for five days, dropped rapidly to normal on the sixth day, and remained there except for an occasional elevation to 100.5° F. during the latter part of the second week in the hospital. Parenteral fluids were administered on the third day because of evidence of dehydration. The child took fluids poorly and vomited persistently. The serum chloride level was found to be 72 milliequivalents (normal 103 to 107 milliequivalents). Coincident with the drop in temperature he appeared brighter, became quieter, mentally alert, and responsive. Two weeks after entry he seemed well, and the strabismus had disappeared. Three weeks after entry the cerebrospinal fluid appeared normal and there were five mononuclear cells per cubic millimeter. The same was found one week later. Physical examination four weeks after entry was normal except that his knee jerks were slightly hyperactive and he tended to walk with a "stiff-legged" gait. He was discharged at this time and at a follow-up visit two weeks later seemed entirely well.

STUDY OF THE CAUSATIVE ORGANISM

The organism was a gram-positive bacillus, 1 to 2 μ in length and about 0.6 μ in width. Different cultures showed slight variation in

the length of the organism. In forty-eight-hour cultures, about one-half the organisms lost the property of retaining the gentian violet when stained by Gram's method. It was not acid-fast, and no spores were seen. Motility was demonstrated by the hanging drop preparation in a seven-hour dextrose broth culture at room temperature. A monoflagellum was seen after staining by the Leifson method.[4] The growth in a semisolid medium showed the "test-tube brush" appearance described by Seastone. The colonies were small, smooth, faintly gray, and nearly transparent on plain agar. Better growth with slight hemolysis occurred on blood agar. In twenty-four hours, the growth in broth was uniformly turbid and a slight sediment was present. Growth was obtained on all the ordinary media. Gelatin was not liquefied, nitrates were not reduced, indol was not formed, and blackening of lead acetate medium was not observed. Growth was abundant under anaerobic conditions. Dextrose, dextrin, rhamnose, salicin and galactose were fermented in twenty-four hours without gas formation. Lactose was fermented in forty-eight hours and saccharose in six days, but no gas was formed. No change occurred in mannite and dulcite after two weeks' incubation.

One cubic centimeter of a twenty-four-hour broth culture of the organism injected intravenously had no visible effect on a chicken. No change was noted in a guinea pig after injection of 0.05 c.c. A rabbit survived an injection of 0.2 c.c. A mouse died forty-eight hours after receiving 0.05 c.c. of the culture intravenously. The organism was recovered in pure culture from the heart's blood, and no gross abnormalities were noted in the organs.

Seastone[5] observed the blood leucocyte response of a rabbit after the intravenous injection of 0.15 c.c. of a twenty-four-hour broth culture of this organism. The total leucocyte count was 6,200 cells per cubic millimeter preceding the injection. The differential leucocyte count showed that 6 per cent of these cells were monocytes. Daily counts were made, and the monocytes were noted to increase, the maximum appearing on the fifth day after the injection. At this time the total leucocyte count was 13,000, 27 per cent of which were monocytes.

The immunologic relationship of this organism to the other members of the genus Listerella was studied by Seastone.[5] The following agglutinating titers were observed:

SERUM PREPARED AGAINST	HOMOLOGOUS TITER	TITER WITH THIS ORGANISM
Fowl strain	1:5000	1:2000
Human strain	1:5000	1:5000
Bovine strain	1:2000	1:2000
Sheep A strain	1:5000	1:5000
Sheep B strain	1:5000	1:5000
B. monocytogenes	1:10,000	1:320

The agglutinating power of the patient's serum for the organism was tested two weeks after admission. There was a definite prozone with no visible agglutination in the serum dilutions of 1:20 and 1:40. Definite agglutination was observed in a dilution of 1:80 to 1:640. Two weeks later no agglutination was observed in any dilution of his serum.

This organism was found to agglutinate in normal horse serum, a property described by Seastone for other members of the group. Five samples of horse serum were used, and agglutination was noted in all of them in a dilution of 1:640.

DISCUSSION

Several points may be mentioned concerning this organism. Human infection with a member of the genus Listerella has undoubtedly occurred more often than reports would indicate, and in all probability such organisms may have been classed as members of the diphtheroid group. The agglutination of the organism in normal horse serum suggests that this might prove of value as a diagnostic aid in establishing the identity of similar organisms if found in human or animal infections. It would seem from the few experiments done that this organism is not very virulent for animals. It seems fairly certain that the organism described can be classed as a member of the genus Listerella from the cultural, morphologic, and immunologic relationships to the other members of the group.

SUMMARY

A case is reported of acute cerebrospinal meningitis with recovery in which the causative organism apparently was a member of the genus Listerella. The morphologic, cultural, and immunologic relationships of this organism to other members of the genus Listerella are described.

I wish to express my gratitude to Dr. C. V. Seastone, of the Rockefeller Institute for Medical Research, at Princeton, N. J., for many valuable suggestions; for his permission to publish the agglutinating values of this organism with the antiserums prepared against the other members of the genus Listerella, and for the figures representing the blood monocyte response of a rabbit following intravenous injection of the organism.

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BANANA POWDER AND THE FECAL FLORA OF INFANTS

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DURING the past decade considerable interest has centered around the use of banana, both fresh and in the powdered form, in infant feeding. The digestibility of these products has been amply demonstrated, but aside from this feature other interesting and as yet unexplained facts have come to light. For example, the almost specific action of banana in cases of celiac disease and the peculiar tolerance of the diabetic patient for banana carbohydrate.

Taking cognizance of these facts, we are naturally interested in knowing why they are so. In the case of the diabetic we are at a loss even for an approach to the problem, whereas the celiac child with his derangement of digestion, metabolism, and intestinal bacteriology offers a more fertile field for investigation, albeit cases of celiac disease are now great rarities.

Haas[1] was the first to introduce banana powder in the diet of patients with celiac disease and demonstrated a marked improvement in these children. Their tolerance for the fresh fruit, for example, was such that in certain instances as many as forty bananas a day were eaten with relish and without intestinal disturbances. Surely that shows a remarkable tolerance. What, then, is the effect, if any, of banana or banana powder on the intestinal flora of infants?

Kahn[2] reported observations on the changes in the fecal flora of seven normal infants receiving, after a preliminary normal diet control period, formulas in which an ordinary carbohydrate (5 per cent cane sugar) was changed to 5 per cent banana powder. He noted a change in the flora of from 0 per cent gram-positive organisms during the control period to 90 per cent or over, gram-positives after twenty to twenty-five days of the diet with the banana powder supplement. Such observations in the normal infant would suggest a possible explanation of the action of banana carbohydrate in celiac disease.

In this study we have attempted to duplicate, if possible, Kahn's results, adhering closely to his technic and method of feeding with only slight modifications. Our group consisted of ten infants ranging in age from one week to eight months, all normal with respect to their gastrointestinal tracts and free from other disease; they were chosen principally because they were to remain in hospital for a sufficient length of time to enable us to complete the study.

Method of Procedure.—During our preliminary control period, which ranged in duration from ten to thirty-four days, with an average of

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twenty-one days for the ten babies, all the babies, except two, received formulas of evaporated milk, corn syrup, and water, the carbohydrate being added to total 8 per cent. The two exceptions noted received dextrimaltose in place of corn syrup. All were gaining satisfactorily and were normal in every respect, though one had a harelip, which necessitated spoon or tube feeding.

Bowel function was normal in all and remained so throughout the experiment.

Stools were collected in the diapers, at least two each week being examined. With a sterile applicator a small portion of the feces was taken from the center of the stool as soon as passed, and this was emulsified in a solution of 0.8 per cent salt solution containing 0.5 per cent formalin to retard growth of living organisms. The staining properties of the organisms were not affected by the formalin as proved by specimens suspended in saline without formalin.

The suspensions were allowed to stand until coarse particles had settled out; the supernatant fluid was then poured off and centrifuged at high speed. Fluid was again decanted, and smears were made of the sediments and stained by Gram's method; acetone was used as decolorizing agent.

Counts of the organisms were made in various parts of the smears, from 300 to 500 organisms being counted on each preparation.

Table I gives the average percentages of gram-negative organisms

TABLE I

CASE NO.		NO. DAYS	NO. STOOLS EXAMINED	AVERAGE % GRAM-NEGATIVE ORGANISMS	EXTREME % GRAM-NEGATIVE ORGANISMS
1	C*	32	7	76.4	60-90
	E	64	11	71.8	20-95
2	C	32	8	79.3	60-95
	E	44	12	79.6	55-95
3	C	30	7	88.5	75-95
	E	27	9	82.2	65-95
4	C	20	6	84.1	65-95
	E	52	15	76.6	40-95
5	C	10	3	85.0	80-90
	E	21	10	71.5	30-90
6	C	21	7	77.9	60-90
	E	15	6	80.0	65-90
7	C	27	6	85.0	65-95
	E	63	8	67.5	35-85
8	C	17	5	78.0	60-90
	E	20	10	71.0	40-95
9	C	15	3	71.0	65-80
	E	22	5	73.0	60-85
10	C	11	4	70.0	50-95
	E	10	3	65.0	50-80

Average of all stools in control period, 79.5% gram negative.
Average of all stools in experimental period, 74.8% gram negative.

*C, control period.
E, experimental period.

in all stools examined for each of the ten cases during the control and experimental periods, as well as the extremes found.

It will be noted that there is very little change toward gram-positiveness in the entire series, the general average showing less than 5 per cent swing from the gram-negative to the gram-positive. It will further be noted, however, that nowhere in the control period did we find the low extreme of gram-negative organisms that we found during the experimental period. Thus Case 1 on the fifty-sixth day of the experiment showed only 20 per cent gram-negative, although seven days later another stool gave 70 per cent negatives. In another instance (Case 4) the gram-negative organisms reached the low level of 40 per cent on the forty-seventh day of the experiment, but four days later 90 per cent of the organisms were gram negative. This great variation was noted throughout the series.

In reviewing the work of other investigators in their attempts to effect an alteration of the human intestinal flora, one is impressed with the difficulty with which this is attained. Introduction of live cultures of *B. acidophilus* or *B. bulgaricus* into the food has not met with success, for these organisms are feebly viable, if at all, in their passage through the gastrointestinal tract. Indeed Park and his associates[3] are doubtful if any nonautogenous strains of organisms can be successfully implanted in the human intestinal tract.

Some authors have found that feeding diets high in lactose has changed the flora from gram-negative to gram-positive, but the results were variable. Fructose also effects such a change.

In this study we have been entirely unable to obtain results similar to those of Kahn, even though we carried out our work along almost identical lines. He used cane sugar in his control period, we used corn syrup or dextrimaltose; but it is difficult to understand in what manner this would influence our results to differ so markedly from his. The fact that we added 0.5 per cent formalin to our saline suspension fluid was proved by controls to make no difference in the percentages of gram-positive and gram-negative organisms.

Referring once more to our Case 1 in Table I, we see that after sixty-four days on the diet supplemented by banana powder the average percentage of gram-positive organisms found in the examination of eleven stools during the period increased only 4.6 per cent over that in the control period. In the entire series of ten cases the change to the gram-positive side was only 4.7 per cent—a figure within the limits of experimental error. Attention is called to Cases 2, 6, and 9 in Table I, which showed an actual increase in gram-negative bacteria during their experimental periods of forty-four, fifteen, and twenty-two days, respectively. Kahn's patients received 5 per cent banana powder in a two-thirds milk formula, a total of 8 per cent carbohydrate. In our

series of ten cases the formulas represented one-half whole milk (2.25 per cent lactose) with banana powder to bring the total carbohydrate to 8 per cent (5.75 per cent added banana powder). We, therefore, used more of the powder than did Kahn.

CONCLUSIONS

1. Banana powder forms an easily digested carbohydrate addition to a formula for an infant.
2. Gain in weight is just as good as or better than it is with other carbohydrate.
3. There is a slight tendency for the fecal flora to change toward the gram-positive strains, but this change is variable and in the main insignificant.
4. Irrespective of the type of feeding, age, and weight of the patient, there normally occurs a variation in the fecal flora.

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Pediatric Clinics

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THE University children's clinic of the Charité is the oldest in Germany and looks back on a history of over one hundred years. In the year 1829 a special children's department was organized, which from the beginning was conducted as a policlinic for sick children. The first head of this new department was Wolff, but after a year Stephen Frederick Barez, who instituted the first clinical teaching in the department, was placed in charge. Two years after his death Privat-Dozent Dr. Hermann F. L. Ebert took up the clinic and out-patient instruction and, according to the annals of the Charité, directed the department in a praiseworthy manner for thirty-three years. After his death Edward Henoch was called from many applicants to the vacant position. Henoch may well be called one of the "early masters" of our specialty in Germany. Under his leadership the clinic grew from year to year. In the early eighties the number of new out-patients reached 4,000 annually.

After Henoch's retirement with emeritus rank, and after it had been conducted for one semester by the well-known internist Karl Gerhardt, Otto Heubner took charge of the clinic. Heubner at first, like his predecessor Henoch, represented his specialty only as an *extraordinarius,* but after a year became *ordentliche* professor. It appears that Virchow chiefly was opposed to establishing this new professorship.

Heubner was the founder of clinical pediatrics in Germany. His masterly textbook received a remarkable distribution. One can even today read with profit his presentation of the infectious diseases. Heubner was an outstanding teacher who founded a great school among whom the names of Finkelstein, Langstein, Rietschel, Reyher, Kopfe and Stoeltzer may be mentioned.

The old clinic which Heubner took over was certainly no model in its physical aspects; in any case on his official acceptance he characterized the department as "miserable" and the lecture hall as "awful." A new clinic was erected according to his plans and occupied in 1903. In general, this children's clinic, which is in use today, was modelled after the Leipzig university clinic which was also erected by Heubner.

Heubner's gifted successor was Czerny. He is the founder of German science in the field of infancy, the fundamentals of which he had already laid down at the time of his appointment. Czerny's work brought German pediatrics to its highest place, and he was most successful both as an investigator and as a teacher. In 1933 he retired, and George Bessau was called to the chair; he like Heubner had previously been in charge of the Leipzig clinic.

The interior arrangements of the clinic have been considerably altered since Heubner's time, but the outside remains almost unchanged. Consequently the bed capacity of the Charité children's clinic—somewhere about 120—cannot compare with some of the large Berlin children's hospitals. It is not its purpose to give medical care to the largest possible number of children, but rather the chief function of the clinic is investigation and teaching. This gives direction to the character of clinical material admitted.

The nucleus of the clinic consists of a main building with three wings extending to the north, south, and west respectively (Fig. 1). On the ground floor of the north wing is the infant division, which is divided into many rooms. One ward in this station has recently been reconstructed into glass-enclosed cubicle wards. A small wet-nurse ward is attached to the infant division to care for the nursing mothers with infants. There is also a milk kitchen with the most modern cooking and sterilization apparatus (Fig. 2.) In connection with the infant division there is a room *Klimakammer*, where temperature and humidity—independently of one another—can be varied within wide limits with the aid of exact measuring apparatus.

The division for older children is located on the first floor of the north wing and consists of two large wards and necessary side rooms. One ward opens directly

Fig. 1.

on a roof garden. The children's division, among other modern apparatus, contains one for underwater intestinal irrigation.

The second floor of the north wing contains the living quarters for nurses.

Between the north and south wings a connecting building built in 1932 contains the milk kitchen and the roentgenologic laboratory. The latter contains the most modern apparatus for diagnosis and for superficial and deep therapy. It is completely protected for high tension and rays, which is most important for a roentgenological department for children. Apparatus for diathermy and "short wave" are also located in this department.

The south wing of the main building contains the out-patient department with a large waiting room reached directly from the street so that the out-patients do not enter the clinic itself. There are six fully equipped examining rooms completely separated from one another for physicians. The library is on the first floor of the south wing as are the spacious chemical laboratories for research. The bacteriologic laboratories are on the third floor. The single rooms are small but practically arranged so that they meet the needs.

Fig. 2.

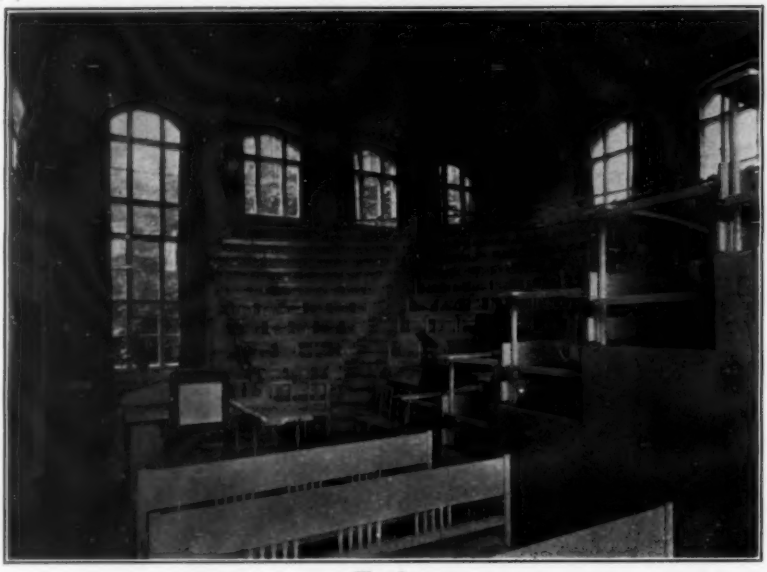

Fig. 3.

The west wing of the main building contains the auditorium which was erected by Czerny (Fig. 3). It has a special entrance for students and contains 234 seats; this seating capacity can be increased by benches, but in spite of all measures the auditorium is not large enough to hold the student body. Above the audi-

torium are the rooms of the clinical director, the modern physical-chemical laboratory, and living quarters for physicians.

In the garden behind the main building is a quarantine station built of stone, as well as three wooden barracks for the care of children with infectious diseases. The wooden barracks, which today are in a bad condition, have an historical interest in that they were erected more than forty years ago in order to give Robert Koch the opportunity to assemble clinical experience with the tuberculin he discovered. In the coming year these barracks are to be torn down and replaced by modern new buildings. There is also a small animal house in the garden.

The ordinary clinical procedures are carried out in a small laboratory which is attached to each ward of the clinic. Thus routine clinical work is separated as far as possible from the laboratories for scientific investigation.

Two *Oberärzte* assist the director, one of whom is a qualified university teacher who shares in the clinical teaching. In addition, there are four assistant positions which are held by physicians who have been thoroughly trained in one of the basic medical sciences (physiologic chemistry, physical chemistry, bacteriology, etc.) Further there are staff physicians who serve from one to three years and temporary assistant physicians from the army who are assigned to the clinic as *praktikants*. This comes from an old tradition of the Charité, which, according to the purposes of its founder, Frederick Wilhelm I of Prussia, was intended solely for the training of military surgeons.

There are further three appointive assistant places, a large number of voluntary assistants and medical *praktikants*, and foreign physicians from different countries who work in the hospital for longer or shorter times. For the scientific workers, four technical assistants are available.

In addition to the clinical instruction for the students, each year postgraduate courses for practitioners, pediatricians, and public health physicians are held, so that one of the chief functions of the clinic, to serve as a teaching institution, is completely fulfilled. As regards the second function, scientific investigation, the tradition is similarly well taken care of; it is the will of the clinic to maintain and add to its honorable heritage.

Critical Review

INFECTION AND IMMUNITY

Local Infection and Immunity

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INTRODUCTION

In a previous review on infection and immunity,[1] I briefly alluded to specific local immunization, a subject that has been emphasized by the recent experiments and writings of Besredka,[2] who has compiled his views on this subject in a small volume.

There have been many theories of immunity and protection. One of the oldest was the exhaustion theory of Pasteur, who believed that organisms exhausted the material necessary for their growth so that no food remained, and hence reinfection was impossible; another was the retention theory of Chauveau, who said that organisms left products of their own metabolism in the host that were noxious to any subsequent bacterial growth. There was also the reenforcement theory of Buchner; the osmotic theory of Baumgarten,[3] who hypothecated that disturbances in osmotic equilibrium caused bacterial death; and the alkalinity theory of V. Behring,[4] who predicated that there was an association between the alkalinity of blood and its bactericidal action. Some of these theories have never been completely disproved even though they are not now accepted.

Although Metchnikoff was preceded by others who held the same belief, he was the first to give scientific evidence to support the contention that protection and subsequent immunity were the results of a battle between the cells of the host and the noxious elements. To describe this battle he coined the term "phagocytosis." The reaction on the part of the host was a cellular one, and the immunity that developed was cellular immunity. Although he persistently maintained his original hypothesis, he was forced to admit some modifications. To him and his coworkers, the body cells were the first and last factors in the mechanism of defense. To them, all other things, including antibodies, were formed in the cell and an excess of the latter in the circulating blood stream was merely evidence of a momentary overflow of elements that had originated in the body cells and had been shunted off into the blood stream, a condition that was seen with massive infections.

Metchnikoff believed that the microphages (polymorphonuclear cells and, to a lesser extent, the lymphocytes and eosinophiles) and the macrophages were the particular cells that protected an individual and the ones that had to do with immunity. The latter cells are found in vari-

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ous places and include the large mononuclear leucocytes, the ameboid cells of the spleen and lymph glands, Kupffer's cells, endothelial cells, histiocytes, clasmatocytes, bone corpuscles, wandering cells, giant cells of the bone marrow, certain embryonic cells, etc. Many of these terms are applied to the same cell, but, irrespective of terminology, all of them are at least homologous as regards their phagocytic activity, and probably all of them belong to what is termed "the reticuloendothelial system."

The site of antibody production might probably be in the lymphatic organs, spleen, bone marrow, or liver, etc. Hence they would concentrate in the spleen or liver, etc., and be present there before being found in the blood stream. Hektoen, however, has shown that the removal of the spleen does not alter antibody production, a conclusion also reached by Karsner, Amiral, and Bock. Could it be the liver? Although Violle showed that by injection of the gallbladder antibodies were produced more rapidly, the conclusion that the liver was the organ that formed antibodies could not be accepted since Hektoen and Curtis have demonstrated that the removal of one-half of the livers of rats did not alter the production of anti-red blood sheep cell antibodies. In fact, there was no material difference between the production of antibodies in the animals operated upon and in the controls. Thus it could not be said that immune bodies arose in either the liver or the spleen.

Opposed to Metchnikoff was the Humoral School led chiefly by Flügge, Bordet (partially), and Nuttall. Like these workers, Weil felt that immunity depended in a large part upon the protective power of the blood and bodily fluids. This school believed that humoral antibodies were formed in the fluid tissues of the body and that the local process itself had little or nothing to do with protection. A vast amount of fundamental research was produced by this group. The fact that antitoxins actually helped combat diseases gave them a large following.

So far as the subject reviewed here is concerned, it is easy to see that local immunity would tend to eliminate the necessity of even considering a humoral factor, and the production of antibodies would have to be explained in some other way than after the fashion of humoralists.

STAPHYLOCOCCUS AND STREPTOCOCCUS

In 1923 Besredka[5-7] stated that the application of specific broth dressings produced a specific generalized immunity in rabbits and guinea pigs which protected them against the effects caused by the injection of streptococcus or staphylococcus organisms. This immunization was brought about either by injecting the sterile specific broth filtrate made from a culture that was grown for ten to fourteen days, reinoculated and again filtered, or by injecting a vaccine of a specific culture grown for only twenty-four hours. This vaccine was previously heated to 60° C. for thirty minutes before injection. Immunization was likewise accomplished by applying compresses to the skin, of either the sterile specific broth or the heat-killed broth vaccine. Brocq-Rousseu, Forgeot, and Urbain[8] repeated and confirmed these experiments. Citron and Picard[9] and Picard[10] used polyvalent broth filtrates with good results in cases of erysipelas, furunculosis, carbuncles and osteomyelitis.

It was not long before experiments were begun to test Besredka's observations on "specific pansements," specific dressings as applied to skin infections, especially infections caused by staphylococcus and strep-

tococcus organisms. Gratia[11] obtained the same results as Besredka with nonspecific broth. Mallory and Marble[12] injected sterile specific and nonspecific broth into rabbits intracutaneously and immunity that followed against staphylococcus was comparable in both instances. Miller[13] reported the same results with specific and nonspecific broth filtrates, vaccines, horse serums, and meat broths. Gay was responsible for most of the work that showed that clasmatocytes can offer an effective barrier to bacterial invasion. Freedlander and Toomey[14] also showed that plain broth is just as effective as specific broth filtrate when applied as compresses on the skins of guinea pigs to protect them against the subcutaneous injection of lethal doses of *Staphylococcus aureus*. They showed that plain broth practically always alters the inflammatory reaction, that this protection was not specific, that it was localized, and that it was self-limited. They showed that in the animal protected with plain broth there was an increase in clasmatocytes and fibroblasts with a dense exudation of polymorphonuclear cells, the latter, in the main, not having degenerated. The clasmatocytes phagocytosed the bacteria early, and it seemed to the authors that there was a relative proportion between the number of clasmatocytes on hand before infection started and the resulting immunity. Imschenetzky[15] worked with topical applications of Besredka's broth made from cultures of staphylococcus and stated that his conclusions were the same as those of Freedlander and Toomey. He noted leucocytes in the epithelial layer and was unable to find much fibroblastic proliferation. Toomey and Freedlander[16] then performed numerous experiments with various materials and proved that many substances, such as plain broth, 10 per cent peptone, 1 per cent peptone, Liebig's meat extract, mustard plaster, and normal horse serum were efficient in protecting guinea pigs from the effects of massive doses of *Staphylococcus aureus* injected subcutaneously. They showed likewise that no matter what the stimulus, the local effect was the same. They also showed that topical applications of such substances as saline, water, and simple dry compresses gave some protection, but to a lesser comparable extent. They showed that neither Besredka's specific broth filtrate nor plain broth protected the experimental animal if applied at the time of inoculation or thereafter. Such experiments as described can admit of only one conclusion, i.e., the protection as described by Besredka as being specific is nonspecific in nature, is not general, is probably due to a cellular reaction, and is strictly local in character.

Clasmatocytes were first definitely linked with immunity by Gay and Morrison,[17] and Gay and Clark.[18] They found that infusion broth or diluted egg white injected locally produced a marked increase in the number of these cells in the pleural cavity of rabbits and that such animals were protected against many times the fatal dose of streptococcus when subsequently injected intrapleurally. In the normal animal, the number of streptococci increased until its death (five to seven days) following the injection, while in the broth-injected animals, the culture made from fluid withdrawn from the pleural cavity was sterile in from three to four hours. Substances such as aleuronat, which produces mostly an increase in polymorphonuclear leucocytes, gave no such protection. Rivers and Tillett[19] found that small areas of skin infiltrated with either normal serum or meat infusion broth proved more refractory than normal skin to infection with hemolytic streptococci. They concluded that the refractory state evidenced in the tissues was non-

specific in character. They thought, however, that greater local protection was afforded by the infiltration with homologous immune serum than with normal serum. In unpublished work, Toomey and Freedlander[20] found essentially the same results with streptococci as they did in their experiments with the staphylococcus organisms.

It can be said that the vast amount of evidence seems directly opposed to the belief that there is any value in the so-called specific dressings of Besredka as such. It can be pointed out that as far as the streptococcus and staphylococcus organisms are concerned, local protection does not give rise to general immunity. But the important question is: Is the skin a place where local resistance is better than elsewhere or does the skin possess some purely individual property which makes it more efficient than any other organ of the body for the destruction of streptococci and staphylococci? It would seem that the chief protection the skin affords is merely mechanical, and, once a break occurs, infection is disposed of just as it is elsewhere and in the manner described by Gay, i.e., by the quick mobilization of certain cells of the body and to a lesser extent of the local bodily fluids.

TYPHOID FEVER AND DYSENTERY

The portal of entry for typhoid fever organisms is stated as being by way of the gastrointestinal tract. Besredka asserted that rabbits are ordinarily immune to infection per os, and that when they are injected intravenously with organisms, the latter are localized in the gallbladder, in the upper intestines, and at times in the entire intestinal tract. From macroscopic examinations he concludes that typhoid and paratyphoid infections do not take place in the blood stream, but principally along the intestinal and biliary tracts. Since rabbits are not sensitive to these virulent bacteria per os, it is necessary to have some factor which when added would make the bacteria more resistant or the intestines less resistant. Fasting rabbits were given ox bile, and it was found that this reduced in a large measure the natural resistance of the animal to paratyphoid infection. The reaction to ox bile is local, but, after it has been given, infection may take place by routes ordinarily not infective. Even then such infections are localized in the intestines and gallbladder, proving again that the intestinal wall is the local receptive organ. Bile by cholagogic action removes the superficial layer of cells; the mucus is swept on, and the intestinal wall is easily penetrated. Since at such a time there is a break in the local defense of an organ that is naturally immune, paratyphoid given per os may infect. Besredka infers that natural immunity against paratyphoid is produced locally. Sedan and Herrmann[21] confirmed Besredka's results when using typhoid as the test organism. No matter where bacteria were introduced, whether in the mouth, the muscle, the vein or the subconjunctival area, the result was the same—a local involvement of the intestine. Since the intestines are denuded of mucus, the bacteria or their products come in direct contact with the receptive cells under the mucosa and infect them. It should be easy to bring these cells into contact with a dead specific antigen and immunize them or make them nonreceptive or desensitized. Immunity may follow the injection of antigen, and, if the disease has a local portal of entry, perhaps the latter could be immunized locally. The way to do this would be per os. Especially would this be logical if, as Besredka claims, subcutaneous immunization is not always efficient.

Reports shortly appeared, one by Sarthe in 1922 and another by Cantacuzene and Panaitesau in 1924. The latter stated that both the methods of vaccination, per os and by subcutaneous injection, were efficacious. Zingher and Soletsky[22] could not immunize their animals following the procedure of bile feeding. Gay[23] asserted that Neri, Teale, and Gye likewise failed to obtain immunization in animals.

One is inclined to think that the cells of the gastrointestinal tract have not been given their just due. The inherited natural resistance also should be considered. It would not seem illogical to suppose that the infection of dysentery, paratyphoid, and typhoid fever are infections which give similar pathologic effects in a relative measure, the severity of which depends on the potency of the endotoxin produced by the various organisms. In dysentery an endotoxin is produced and easily liberated, producing typical lesions. The enteric organisms are also able to produce highly potent toxins easily (Ecker and Rademaekers,[24] Ecker,[25] Ecker and Biskind[26] and Toomey[27]). It could be conceived that the gut has developed a high degree of immunity to the enteric organisms that are usually present, i.e., against the colon bacilli and their close generic bacterial relatives so that actual infection in the human being results only when the gut is massively infected. On the other hand, individuals usually have no natural immunity to dysentery. Consequently, it is logical to theorize that a small amount of this toxin could cause a great amount of damage. A comparable amount of damage could only be caused by a large amount of typhoid toxin. I do not see how one can conclude definitely that dysentery produces a more potent toxin than paratyphoid. To demonstrate the comparable effects of toxins necessitates the use of a suitable animal comparably susceptible to both toxins and hence not immune to either. But the important point is that the intestine, like the skin, has a covering which mechanically protects it. When this covering is removed, infection may enter, an infection which is combated here the same as elsewhere by the local mobilization of cells.

Besredka thought that the lesions of dysentery were limited to the intestine, no matter whether the inoculation was made with living or dead virus, or endotoxin, and irrespective of the portal of entry, whether intravenous, subcutaneous, or per os. His arguments are similar to those used in his observations on paratyphoid. He thinks that the intestine bears the same relationship to the dysentery bacillus as the skin does to staphylococci and streptococci. He states that the subcutaneous inoculation of dysentery bacillus is a relatively inocuous procedure. He decided that it would be practicable to vaccinate human beings by mouth, and he quoted a number of interesting clinical experiments. Combiesco, Magheru, and Calalb[28] and Enlows[29] confirmed Besredka's contentions and were able to produce immunity when Shiga's bacillus was ingested. Others obtained good protection by other routes—through the skin (Balteanu[30]) and subcutaneously by Enlows[29] and Ciuca and Balteanu.[31] Gay[32] states that Neri, Glotoff, and Webster found that bile made animals more susceptible to the dysentery bacillus but that Webster could not determine that they could be immunized per os after such a procedure.

Irrespective of the fact that the subcutaneous route of immunization may be better than the gastrointestinal route, the fact still remains that laboratory animals and human beings may be immunized by using the latter portal of entry.

ANTHRAX

Besredka's experiments in anthrax may be summarized as follows: Anthrax does not affect a susceptible animal unless the organisms are introduced through the skin. If injections are made subcutaneously, intravenously or intraperitoneally in animals, there usually are no reactions even when large doses of organisms are injected. On the other hand, even the smallest dose injected intradermally will bring about the disease. When organisms are injected elsewhere than into the skin, the fact that the animals may die does not rule out the skin as the local portal of entry since the injecting needle must pass through the skin and in so doing it infects the skin either on its way in or out. The skin would be the local organ affected and it would follow that protection against anthrax should come about by protecting the skin. Besredka accomplished this by topical applications of specific broth dressings, after which he found that the animals were immune to anthrax, no matter where they had been injected. He attributed such immunity to two factors: (1) the immunity of the skin acquired by local cutaneous vaccination, and (2) the natural refractory state of all the other organs. His experiences are bolstered up by the practical experiences of several authors mentioned in his book.[2]

When his experiments are analyzed, however, especially in view of the importance given to certain cells by the researches of Buxton, Torrey, and Gay and their associates, it is found that another explanation may be even more logical and may in fact definitely refute some of Besredka's contentions. Two things must be kept in mind. The first is the possibility that the cells concerned with protection are more mobile in the peritoneum, blood, etc., and are less likely to be easily mobilized in the skin; consequently, the organisms can grow in the skin for a time without opposition. The second point concerns the manner in which the anthrax bacillus grows and adapts itself to changing environment. Combiesco[33] has shown that under normal conditions the anthrax bacillus is unencapsulated. Combiesco and Dumitresco[34] demonstrated that when unencapsulated anthrax organisms were injected intradermally, infection always occurred; not because the skin was more susceptible, but because sufficient time had elapsed after the injection to allow the organisms to become encapsulated. When the organisms become encapsulated, they multiply unimpeded since the bacterial cells are then resistant to phagocytes. Gratia injected encapsulated organisms intravenously and the animals succumbed, although they did not die when unencapsulated bacteria were thus injected. Besredka could not immunize animals via the intraperitoneal route with his unencapsulated organisms. On the other hand, Supniewski[35] (quoted by Gay) killed the virulent or encapsulated organisms with phenol and was easily able to immunize animals by intraperitoneal injections. Gay reported that areas with relatively slight blood supply, such as the "testicle (Sani), brain (Adeheim and Katku, Cernainu) or muscle (Basset), are at least as susceptible as the skin." He briefly summarized the situation thus: "Skin susceptibility to anthrax is not specific, but a relative absence and slow mobilization of protective cells and fluids in that area allow cultures of sufficient virulence to adapt themselves (capsule or aggressin formation?) and become invasive."

COMMENT

The idea that most microorganisms have a distinctive portal of entry is not new. Staphylococcic and streptococcic infections tend to be localized to the skin, but that they may cause reactions in the human being when taken per os has been shown by Jordan.[36] Should the infection caused by these organisms not be localized then a grave situation would result for the patient, even though such a localization may occur possibly elsewhere. After the skin is penetrated, the reaction is locally the same as would follow an injection through a needle elsewhere, the tempo of phagocytosis probably depending upon the ease with which cells can be mobilized. These comments, of course, apply only to non-immunized areas and to primary infections and do not take into consideration the mechanism of passive immunity.

It has also been recognized that diseases like typhoid, dysentery, and the like usually enter the body through the gastrointestinal system.

That there may be a condition of local organ resistance has long been recognized, since, as Besredka has stated, the immunity which may develop in one ocular conjunctiva does not necessarily extend to the entire animal. Not only are other animal organs not protected following the vaccination of one cornea, but the immunity acquired in the prepared conjunctiva may not even extend to the other eye.

Even were it conceded that most of the diseases discussed have their natural portal of entry in the manner stated, nevertheless, the mechanism of immunity should still be predicated upon cell activity. Virchow's dictum that all cells come from cells could be paraphrased in a sense, and with reference to immunity it might be said that protection must ultimately come from cells, or that only cells and their products protect the host. Metchnikoff called attention to his microphages, but he did not stress the importance of his macrophages. The phagocytic power of these has been well illustrated by Rous and Jones.[37] In numerous papers Gay and his coworkers have shown the importance of these cells in immunity.

In the light of all that has been said it could be concluded that there may be ways to immunize an individual locally. There may even be areas that because of their anatomic make-up allow bacteria to enter the host more easily. These portals of entry may even be used to immunize the host. It is logical to deduce, however, that basically this local immunity is the result of a cellular reaction and that, when humoral antibodies are present, they are the result of a more than virulent infection or a more prolonged local battle on the part of the cells at the portal of entry. It does not follow that because immunization is possible by local applications or injections, the local area is the sole portal of entry, and that immunization cannot be accomplished elsewhere; nor does it follow that the organs by which bacteria may enter are better equipped to dispose of a noxious agent; and, although antibodies might arise locally, it cannot be concluded that these specific agents can only arise in the organs of entry and nowhere else.

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American Academy of Pediatrics

Proceedings

FIFTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

NEW YORK CITY, JUNE 7, 1935

Round Table Discussion on the Newborn

Special Subject: Nutrition During the Newborn Period

Chairman: Dr. Arthur H. Parmelee, Chicago

Assistant: Dr. James W. Bruce, Louisville

The meeting was called to order at 2:30 P.M., at the Hotel Waldorf-Astoria, by the chairman, Dr. Arthur H. Parmelee, Chicago.

CHAIRMAN PARMELEE.—The newborn has many adjustments to make in the transition from intrauterine to extrauterine life. One of the most important of these concerns nutrition. During fetal life the nutritional requirements are supplied by the mother directly by way of the circulating blood. But from the moment the umbilical cord is severed, the infant's nutrition depends upon his ability to get appropriate and sufficient food into his stomach, and upon the anatomic and functional efficiency of his digestive and absorptive mechanism. As physicians, we are responsible for the feeding technic used in the care of the newborn infant, and to that extent its nutrition depends upon us. A thorough understanding of the various phases of the subject is essential if we are to assume this responsibility with intelligence. The many and widely differing technics in use throughout the country testify to the confusion or the indifference that exists and to the need of a renewal of interest in the subject and a wider dissemination of accurate knowledge.

An initial loss of weight occurs in practically every newborn infant. The amount of this loss varies considerably in individual infants, but the average is 7 to 8 per cent of the birth weight, unless definite measures are instituted to lessen it. The weight curve reaches its low point on the third day in the majority of cases and then starts upward coincidentally with the beginning of true lactation in the mother's breasts.

A disproportion between intake and output adequately explains the bulk of this initial loss although actual combustion of carbohydrates and fats to supply body heat and energy, and probably some other factors, are responsible for part of the weight loss. Only a minor part of the disproportionately large output is accounted for in the urine and meconium; the major portion is water-loss through the lungs and skin as insensible perspiration.

We are accustomed to speak of this initial weight loss as physiologic, but there are those who object to such a designation and prefer to consider it a condition which at least borders closely on the pathologic. The question is largely of purely academic

importance, but it would seem more logical, as Czerny suggests, to consider the peculiarities of the life processes in the organism of the healthy newborn the result of the conditions existing immediately after the birth, partly directly associated with the birth itself, and likewise the result of peculiarities of certain organ functions in the newborn, and to designate them as physiologic. We cannot well consider a symptom that occurs almost without exception in all newborn infants pathologic.

It has been adequately demonstrated by many clinical investigators that the initial weight loss can be reduced by the administration of various food mixtures before the mother's lactation is established. Bachmann studied 511 newborn infants; 50 control infants who received no special feeding care showed an initial loss of 9 per cent, and 40 per cent of them had regained their birth weight by the time they left the hospital. Some type of food was fed to 387 infants from the first day on; the average loss among these infants was 5 per cent of their birth weight, and 69 per cent of them regained their birth weight before their discharge from the hospital. Many other investigators have shown similar sets of statistics, Dwyer and Neff, for example. Recently Kugelmass, who strongly contends that the initial weight loss is not physiologic, fed a solution consisting of 6 per cent neutral gelatin, 3 per cent dextrose, and 0.5 per cent sodium chloride to newborn infants every two hours, and succeeded in reducing the initial loss to 1.7 per cent of the birth weight.

The question now arises whether the reduction of the initial weight loss by supplying food and water in the first days of life is of any significant benefit to the child. We find quite a divergence of opinion on the subject. Some, like Kugelmass, feel that the infant derives much benefit from the procedure, while others, like V. Reuss, feel that nothing is gained, and still others think the procedure harmful because such feeding may make it more susceptible to digestive and nutritional disturbances later on. Bachmann was able to follow a large number of the infants in his series for six to nine months and could see no evidence that in a single instance they had been adversely affected. There are those too who contend that the infant who receives food from the first day on and complemental feedings during the period when lactation is being established will not nurse as vigorously at the breast because of lack of hunger. It has been my definite impression that exactly the opposite is true, i.e., that the infant nurses more vigorously, and thus the maximum function of the breasts is more rapidly attained.

Whatever may be our attitude toward feeding before lactation is established, we are agreed, I am sure, that each individual infant's weight chart should be carefully watched for evidence of deviation from what we consider the normal weight curve. When the initial loss is excessive, more than 10 per cent of the birth weight, or when the curve continues downward after the third day, we can surely no longer consider the condition physiologic but pathologic, and we must look for the cause and institute proper measures for its correction. It is important to know how much breast milk the infant is getting; this can be determined by weighing the infant before and after nursing. This should be a routine procedure in every nursery. Unfortunately it is not always easy to get this done in some of our large charity hospitals because of the lack of help. The amount of breast milk the infant gets is not as important information, however, as is the actual weight of the infant from day to day. Anyone who has watched the weight curves of a large number of infants during the newborn period and has analyzed them with reference to the gain in weight as compared to the amount of food ingested will recognize how impossible it is to make a general statement regarding their food requirements. One infant with a birth weight of 8 pounds will gain satisfactorily on 16 to 18 ounces of breast milk a day, while another apparently equally healthy infant with a birth weight of 7 pounds will gain less rapidly on 20 to 22 ounces a day. Individual peculiarities of metabolism can be the only answer to such discrepancies. Too much reliance should not be placed on the

amount of milk the infant obtains from the breasts as a guide to the amount of complemental food he should be offered. It is the practice in many hospitals to give enough of the complemental food to bring the total quantity of each feeding up to 3 ounces. In view of the lack of uniformity of relationship between gain in weight and amount of food intake such a practice seems too arbitrary; there will be many feedings when the infant would take more and also many when he is satisfied with less, just as is the case when the supply of breast milk is abundant. It has long been my practice to offer 2 ounces of complemental food after the breast feeding and allow the infant to take what he wishes regardless of the amount obtained from the breast.

The subject of nutrition during the newborn period is a complicated one. It has to do with many factors other than the technic of feeding. The health and nutrition of the mother during her pregnancy have been shown to have a bearing on the vitality of the fetus, and the doctrine that the fetus is a parasite on the mother may not be entirely correct. The kind of labor and the amount of trauma and shock suffered by the infant will influence its ability to make the new adjustments. Then there is the matter of heritage, the state of maturity at the time of birth, etc. All of these things make individual evaluation of each infant more important than any standard nursery technic.

I am convinced that improvement in the care of the newborn will depend much more upon our interest in each infant as an individual patient deserving of careful history-taking and careful physical examination than upon familiarity with some popular feeding method, resuscitation apparatus, incubator, or the like.

DR. BRUCE.—During the past year in the various hospitals of Louisville a number of methods of feeding the newborn have been used. The object of these methods has been to reduce the amount of initial weight loss and enable the babies to regain their birth weight in the shortest possible time without interfering with successful maternal nursing and without producing any untoward results.

I have collected figures on six methods of feeding newborn babies, and, while the numbers of cases are not large, their study has proved interesting. In all cases the feeding routine consisted of putting babies to the breast eight hours after birth and every fours hours thereafter for three days. After that some were fed seven times in twenty-four hours, and others were continued on six feedings.

The first three groups of babies were observed simultaneously at the City Hospital; the last three groups were observed at two private hospitals.

The first group of eighty-four babies was given nothing but breast milk and water. Two ounces of water were offered between each two feedings in a nursing bottle, and the baby was allowed to take what he would.

The second group of seventy-three babies was offered 2 ounces of a 5 per cent glucose solution between each two feedings.

The third group of ninety-one babies was offered 2 ounces of a mixture of 6 per cent gelatin, 3 per cent glucose and 0.5 per cent sodium chloride between each two feedings.

The fourth group of one hundred babies was offered a formula consisting of 12 ounces of milk, 9 ounces of water, and 2 tablespoonfuls of dextrimaltose. The first day one ounce was offered after nursing, the second day 2 ounces were offered after nursing, and after that the baby was weighed before and after each nursing and enough complementary formula was offered to make 3 ounces at a feeding and seven feedings in twenty-four hours.

The fifth group of one hundred babies was offered 1 ounce of lactogen solution (1 teaspoon of lactogen to 1 ounce of water) after each breast feeding from the day of birth until the baby left the hospital unless the mother's milk supply was so ample that the baby would not take the complementary feeding.

The sixth group of one hundred babies was offered 1 ounce of 6 per cent beta lactose and 0.2 per cent sodium chloride after each breast feeding for the first two days and after that as a midfeeding.

The time at which the lowest weight was reached was observed in all six groups, and the results are tabulated on Chart I. The glucose-fed group lost weight for the longest time (4.5 days) and the milk, water, dextrimaltose group for the shortest time (3.5 days).

The percentage of weight loss showed the water and glucose groups in marked contrast to the other four. As might be expected, the greatest percentage of weight loss occurred in the group in which weight loss continued longest.

The percentage regaining their birth weight by the tenth day could not be observed on the City Hospital cases because most of them had left the hospital before that time. Of the other three groups the beta lactose cases gave the highest figure.

Observations on the type of feeding on discharge, i. e., breast, formula, or breast and formula, were made on only two groups (lactogen and milk, water, and dextrimaltose). The figures ran closely parallel and are in line with those of other observers.

The incidence of vomiting was not observed in the City Hospital cases. In the other three groups it was negligible, i.e., 1 and 2 per cent. A baby who vomited two or more times on two days while under observation was counted as vomiting.

The incidence of diarrhea was observed in all six groups. A baby who had five or more stools on two days during the observation period was counted as having diarrhea. The glucose-fed babies with 16 per cent presented quite a contrast to the others. Next came the gelatin-glucose-sodium-chloride-fed babies with 8 per cent. It was observed by the nurses that most babies taking this latter mixture had more than the usual number of stools even though they could not be classed as diarrhea and that these babies were particularly prone to develop sore buttocks. This same observation was made on a series of babies in another private hospital not included in the above groups, and the solution was discontinued for that reason.

Several months ago I wrote to twenty pediatrician friends of mine throughout the country and asked them what they thought about the routine use of complementary cow's milk feedings in the newborn. I received replies from nineteen of these. Thirteen, or 68 per cent, were not in favor of such feedings unless babies failed to gain in a reasonable time while six, or 32 per cent were in the habit of using them routinely. Those who did not believe in routine complementary bottle feedings advanced the beliefs that babies were thereby rendered less likely to take the breast hungrily and successfully and also that gastrointestinal upsets were more common. It has also been suggested that early feeding of cow's milk might make babies allergic to it. On the other hand, those who did recommend routine complementary feedings believed that the initial weight loss was thereby reduced and that babies regained their birth weight more quickly. They did not think the feedings made successful nursing more difficult. Several men stressed the importance of individualizing the babies and feeding each according to its needs and deplored the use of routine feedings of any kind. I quite agree with this point of view. However, most of the babies born in private hospitals in this country are delivered by general practitioners many of whom are not adept at infant feeding and many of whom leave the feeding of the babies to the judgment of the head nurse on the obstetric floor. Under such conditions routine feeding instructions are almost a necessity.

Several of the men believed that for the first two or three days it was important not to allow babies to nurse more than two to five minutes at a feeding. I suppose the purpose of this is to accustom the mother's nipples very gradually to the nursing process thereby rendering cracks and fissures less likely and also to avoid fatiguing

CHART I

(BIRTH WEIGHTS OF ALL BABIES 5½ TO 9½ POUNDS)

TYPE OF FEEDING	NUMBER CASES	TIME LOWEST WEIGHT REACHED (DAYS)	PER CENT WT. LOSS	REGAINED BIRTH WT. BY TEN DAYS (PER CENT)	FEEDING ON DISCHARGE			VOMITING (PER CENT)	DIARRHEA (PER CENT)
					BREAST (PER CENT)	FORMULA (PER CENT)	BREAST AND FORMULA (PER CENT)		
Water	84	4.3	9.6	--	--	--	--	--	4
Glucose 5%	73	4.5	9.5	--	--	--	--	--	16
Gelatin 6% Glucose 3% NaCl 0.5%	91	3.9	6.5	--	--	--	--	--	8
Milk 12 oz. Water 9 oz. Dextrimaltose ½ oz.	100	3.5	6.4	44	31	12	57	2	6
Lactogen 1 teaspoon Water 1 oz.	100	4.2	6.4	44	34	3	63	1	0
Beta lactose 6% NaCl 0.2%	100	3.7	6.4	55	--	--	--	1	6

mothers and babies at a time when very little milk can be obtained. However, since this practice is not widespread, I wonder if such caution has been found to be of practical value.

The length of the nursing period is undoubtedly most important. I am sure we have all seen babies urged by zealous mothers and nurses to take more than they wanted with the result that they either vomited or were so fatigued that they did not gain. I think a time limit of twenty minutes should be placed on feedings during the newborn period. If babies do not take sufficient food in twenty minutes, then gavage several times a day or at each feeding is a strength-saving measure which will frequently start a baby gaining.

We find the statement in every textbook on pediatrics that the newborn baby is very subject to dehydration fever and to avoid this contingency fluids should be forced routinely, especially in the first few days of life. However, in one large obstetric hospital the following order has been in force for the past three years: "Fluids only on order of the House Staff if baby shows evidence of dehydration (i.e., temperature is taken twice a day, and fluids are given only if temperature is 100° F. or above. If fever is present, temperature is taken every four hours and discontinued when normal is reached)." In other words these babies get the fluid from their mother's breast milk, and none other just as in the good old days. The results have been remarkable. The hospital statistics show there has been no more dehydration fever than there was before, and just as many babies have regained their birth weight by the time they were discharged.

As to the type of artificial feeding employed, I found on going over the answers to my questionnaire that whole cow's milk or evaporated milk mixed with water and karo, dextrimaltose, or lactose were most popular. A few used lactic acid in the mixtures, and one or two used dry milk powders.

The treatment of diarrhea in newborn infants on artificial feeding has proved a difficult problem to me. Most infants respond quickly to reduction in quantity of food, especially the carbohydrate. Others are benefited by protein milk or breast milk from another mother. However, there are a few who obstinately refuse to digest any feeding that is offered. I have found that removal of such infants from the newborn nursery to their homes and putting them under the sole charge of some one who has had years of experience in the care of young infants has worked miracles. Under such surroundings they will frequently begin to digest formulas they had not digested before and gain steadily in weight where before they had remained stationary or had lost.

DISCUSSION

DR. JOSEPH F. PAULONIS (BROOKLYN) discussed the advisability of a change in the routine feeding hours commonly used, so that the first feeding would be at eight o'clock instead of at six. This he felt would give the mother an opportunity for more sleep. He advocated giving as much artificial food after the breast feeding as the infant would take and reported instances of newborn infants who took enormous amounts of complementary food without suffering any ill effects.

DR. ARCHIBALD D. SMITH (BROOKLYN) raised the question of whether the initial loss of weight is really a detriment to the future welfare of the infant.

DR. CHESTER R. BROWN (ARLINGTON, N. J.) asked whether complementary feeding should be continued after a proper gain in weight has been established, and also whether babies given artificial food in the nursery were not likely to be weaned from the breast too early. He stressed the effect upon the infant's vitality of the economic status of the mother. He made a plea for better hospital charts for newborns, stating that the records in most hospitals are entirely inadequate.

DR. ALTON GOLDBLOOM (MONTREAL) suggested that the American Academy of Pediatrics should aid in an effort to get the nurseries of all obstetric hospitals under immediate and complete control of pediatricians. Proper hygiene such as ventilation, avoidance of infection, etc., are as important as the feeding technic. The average initial weight loss is relatively unimportant, and a pathologic weight loss frequently has its origin in conditions other than inadequate feeding. He felt that physicians needed to go back to a study of the fundamentals of infant feeding and the proper use of simple formulas.

DR. L. O. ASHTON (NEW YORK) felt too much stress was being put on the single item of weight and advocated more consideration of each individual infant as a whole.

DR. M. P. BOROVSKY (CHICAGO) discussed the variation in the quantity of breast milk of individual mothers, and the difficulty of prophesying what a mother will be able to do in the matter of producing an adequate supply after leaving the hospital. He suggested that it is perhaps wise to accustom the infant early to some artificial food. He also raised the question of how long the infant should be allowed to nurse at the breast, stating that infants are frequently fatigued by prolonged nursing.

DR. JOHN C. MONTGOMERY (DETROIT) asked about the relationship to weight loss of the time of tying the cord.

CHAIRMAN PARMELEE.—From the discussion, it is obvious that a thorough review of the standard textbooks dealing with the nutrition of the newborn would benefit us all. Most of the questions brought up here have received careful investigation, and there are too many sides to them to permit of arbitrary answers. Czerny and Keller, for example, have devoted much space in their textbook to a thorough discussion of this whole problem. The subject is also thoroughly covered in several of our American textbooks. The peculiarities of the newborn must become a real part of the knowledge of the man in general practice, as well as the pediatrician, if we are to make progress in this field. A more standard nursery technic, more careful and intelligent medical care for each individual infant, better training of nurses in the technic of newborn infant care, better hospital charts and records for the newborn: these are some of the things we can work for.

Book Reviews

Proceedings of the Third Conference on Psychiatric Education. National Committee for Mental Hygiene, New York, 1936, 120 pages.

The proceedings of the Third Conference which was held in Washington in May, 1935, should be carefully studied by every teacher of pediatrics and clinic chief. The theme was "psychiatric education in the setting of pediatrics." Under the chairmanship of Dr. Adolf Meyer many of our foremost pediatricians and psychiatrists participated in a discussion which does much to clarify objectives, methods, and mutual relationships.

Among the papers of the first session we would stress the importance of Dr. Washburn's discussion of "Opportunities for a Liason between Psychiatry and Pediatrics in a Child Research Institute" for the way in which it presents the essence of present-day thought. In the other sessions the coordination of pediatrics and psychiatry in several of our medical schools as it exists today was presented. Dr. Brennemann has written a foreword, and we can do no better than quote it: "Here is written progress.... Two interests, hitherto more or less divergent.... regarding one another often with doubt and distrust.... have come together in a sympathetic spirit.... with an appreciation of a goal and approach that must be shared.... a mutuality of interest in the mental and physical wholeness of the child." The conference, which was largely arranged by Dr. Ebaugh, was an important one in the history of American pediatric teaching and thought.

Width-Height Tables. Dr. Helen B. Pryor, Stanford University Press, Stanford University, California, 1930, Price, 60 cents.

The Stanford University Press has published in pamphlet and chart form the weight tables based on age, height, and bi-iliac diameter prepared by Dr. Pryor. The value of tables based on some measurement other than height, in order to take body type into consideration, is too obvious to need comment. Tables have been prepared for both sexes for from 1 to 20 years. The only additional instrument required is a pair of calipers. To those who make an intelligent use of body measurements—not to those who use them as a goal or end in themselves or as a determinant of health—the tables are of value.

Medical Papers, Dedicated to Henry Asbury Christian. Baltimore, Waverly Press, 1,000 pages.

This is a volume of over one hundred contributions by the present and past associates of Dr. Christian and the house officers of the Peter Brent Brigham Hospital in Boston. In a striking way those who have come under Dr. Christian's influence have honored him on the occasion of his sixtieth birthday. In the story of his life and work ("An Appreciation" by W. T. V. and "Foreword" by I. C. W.) the reason for the feeling they hold for their "Chief" becomes obvious. *Festschrift* volumes have been few and far between in American medicine as compared with European medicine. We cannot help wondering if this may not lie in the fact that foreign *festschrifts* usually honor a seventieth birthday. When one reads of the work which has given Dr. Christain his well-deserved and honored place in American medicine, the thought comes that perhaps the paucity of commentary volumes for our own leaders lies in the fact that so few of them reach the legendary "three score and ten."

American Pediatric Directory. A Listing of Pediatricians of the United States With Biographical Information. JOE T. SMITH, M.D., Knoxville, Tenn., 1936, American Pediatric Directory Company, 128 pages.

This is the first attempt to assemble in one volume all information about physicians specializing in pediatrics and those interested in this branch of medicine. The information included is quite complete and includes personal data of a professional sort. Listings are made by states and also alphabetically.

The form of the book and the arrangement of the text are good, and the book is easy to read. It is rather large due to the large type used; it might be more convenient in a smaller form.

This volume should be extremely useful to the practicing physician as well as to those interested in pediatric education and the trend of this branch of medicine. The author is to be commended for the care with which he has assembled so much information. Future editions should keep this information corrected and up to date.

Comments

ON June 13 a bronze tablet will be dedicated to the memory of Abraham Jacobi at his summer home near Bolton Landing on Lake George. A small plot of land has been set aside as a park and will be maintained by the village. Here will be placed the tablet together with a memorial seat to Carl Schurz which has stood for a number of years at the entrance to their summer homes. Jacobi and Schurz came to America together and owned a large tract of land at Bolton Landing, where they spent their summers. The funds for the Jacobi Memorial have been provided from the Abraham Jacobi Fund of the Section on Pediatrics of the American Medical Association, and it bears the following inscription:

IN MEMORY

1830 1919

ABRAHAM JACOBI

THE PIONEER

OCCUPIED THE FIRST CHAIR OF PEDIATRICS IN AMERICA
A SCHOLARLY AND BROAD-MINDED PHYSICIAN
ONCE PRESIDENT AMERICAN MEDICAL ASSOCIATION

WHO LOVED THESE WOODS AND WATERS ABOUT HIS SUMMER HOME

ERECTED BY HIS FRIENDS AND COLLEAGUES
THE ABRAHAM JACOBI MEMORIAL FUND
THE AMERICAN PEDIATRIC SOCIETY
JUNE 13, 1936

Dr. Fred W. Schlutz of Chicago, president of the Jacobi Fund, will preside at the memorial exercises. Dr. Isaac Abt speaking about Dr. Jacobi will be followed by Dr. Frederick T. Sondern, president of the Medical Society, State of New York. Dr. George McAneny, of New York, a son-in-law of Dr. Jacobi and member of the executive committee of the Carl Schurz Foundation, will speak about Carl Schurz, and an address will be made by Dr. John H. Finley, of the *New York Times.*

As the American Pediatric Society is holding its annual meeting at Bolton Landing on June 11 to 13, with the members of the Canadian Pediatric Society as guests, a large group of pediatricians will be present to honor the memory of the "Father of American Pediatrics."

AFTER careful deliberation the directors of the American Child Health Association decided last November to wind up its affairs and let it pass out of existence. From the start of the organization in 1908 it held to the plan of working with local, state, and national agencies. With the steady growth of child health work and agencies the time finally arrived when the need for the A.C.H.A. grew less and less. The story of the A.C.H.A. has been told in the last number of its *Bulletin* by Dr. Van Ingen. It is not only the story of the organization through the changing patterns of its existence, but it is also the history of child health work in America during the last thirty years. To most of the older group of American pediatricians it will bring to mind many recollections; to the younger group, who are unfamiliar with the struggles by which child health work has been brought to the present stage with which they are familiar, it will be most illuminating as an historical document. It can be said in all fairness that the Academy of Pediatrics is in part a logical development of the old A.C.H.A. and that had there been no such organization with the ideas and ideals it stood for during a quarter of a century, we question whether there would ever have been an Academy.

AT THE request of the state and provincial health officers of North America, the Children's Bureau this year has taken over the responsibility for planning the annual May Day program, which has been a function of the A.C.H.A. for a number of years. The program this year centered on social security for children with special emphasis on health protection. The objective is to review in each state and community the social security program and plan further development under the leadership of state and local health officers, cooperating with organizations and agencies concerned with child health and welfare. Federal aid is now available for maternal and child health, for crippled children, for extending child welfare services, and for aid to dependent children. Plans have been approved and payments already made to over thirty states for one or more of these activities, and a large number of plans in addition have been submitted and are awaiting approval. The Academy has been cooperating actively with the state committees, and every member of the Academy should help in carrying out the local community program, both as an individual and in connection with the local organizations with which he is connected. Any one unfamiliar with the terms of the grants to the states for maternal and child welfare should obtain Maternal and Child Welfare Bulletin No. 1 from the Children's Bureau.